BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 24 1951

PSYCHIATRY OF CEREBRAL DISEASES*

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The title of this paper is a challenge to the psychiatry of eighty to a hundred years ago and to the old materialistic medicine. At that time every mental disease was supposed to be a cerebral disease. This older point of view was particularly stressed by Griesinger, in Zurich, ninety years ago. He felt quite certain that psychoses without cerebral pathology did not exist, but there were some psychoses the cerebral pathology of which had not been investigated as yet.

If I speak of the psychiatry of cerebral diseases, and if I separate it from the psychiatry of diseases with intact cerebral structure, I have no intention of taking part in a philosophical discussion on the relation of mind and body. I approve, of course, of the modern concept of psychosomatic medicine, which considers both—structure and function, body and mind—as equivalent and inseparable expressions of life itself. My paper, however, is not based on theoretical and controversial philosophies. It is based on the concrete and certain fact that up to the present day we have had to deal on the one side with mental diseases which have a cerebral pathology, and on the other side with mental diseases which, so far as our present knowledge goes, do not. It is also based on the conviction that for practical, diagnostic, and therapeutic reasons it is good to consider the differences of psychopathology of the mental conditions with and without cerebral pathology. In this modest unphilosophical sense we are allowed to speak to-day of the psychiatry of cerebral diseases.

Until the beginning of this century most brain pathologists were psychopathologists, and the reverse was equally true. Since then increasing specialization in medicine has gone far in separating brain pathology and psychopathology. The progress of our knowledge in regard to the correlation between psychopathology and brain pathology has been hindered to a regrettable extent as a result of this separation. We must become conscious of the fact that modern medicine is in need of better and more detailed knowledge of the psychiatry of cerebral diseases. It is handicapped in its progress by the neglect of this discipline by two generations of psychiatrists.

Diagnostic Aims in Psychopathology

The importance of the above statement may be demonstrated by a few examples.

The progress of medicine, of neurosurgery, and of antibiotic therapy in particular has given a tremendous practical value to the early diagnosis of brain diseases. Psychopathological alterations are one of the earliest and most important signs of brain diseases. Understood in the right way, they are of the greatest diagnostic importance. There exists, however, in modern psychiatry a marked tendency to undervalue the psychopathological diagnosis. It is a sound reaction to the unsound habit of earlier psychiatrists of building up nosological systems on a mere speculative basis, and of busying themselves with the differential diagnosis of unnatural and hypothetical disease entities in which there was no practical sense.

The sound tendency, however, to break with a speculative psychopathological diagnosis must not lead to the neglect of the real diagnostic values of psychopathology. If the psychopathological study of a patient can demonstrate whether he is suffering from a brain disease or not, psychopathological findings cannot be ignored. In many cases they will prove to be even more important than neurological, pneumoencephalographic, electro-encephalographic, or spinal fluid findings. I feel that it is one of the important tasks of psychiatry to teach the psychopathological differential diagnosis between mental derangements with and without brain pathology. We are still in need of much more research work in order to simplify and improve the principles of such a differential diagnosis.

The question whether the cerebral localization theory, which was proved to be so useful in neurology, can be applied to psychopathology has often been discussed theoretically—with exiguous results. Many prominent psychiatrists have renounced any further consideration of this difficult question. The dramatic emergence of psychosurgery within the last twelve years, however, demonstrates the practical importance of such a question. Faced with the possibility of treating mental diseases by artificial localized cerebral lesions, we ought to study the effect of localized brain lesions more thoroughly. As the technique of brain surgery improves, our patients and we ourselves want to know what can be done with such an improved technique. Our patients are threatened with all kinds of useless surgical trials if we do not co-operate in studying these questions with modern methods.

There is still another point. The progress of our knowledge of the physiology of the adrenals and the

* Lecture given at the National Hospital, Queen Square, London, on February 13, 1951.

teachings of Selye regarding the adaptation syndrome have stressed the importance of endocrinological psychiatry. There seem to be few endocrinopathological syndromes, however, which cannot be elicited by lesions of the nervous system. Vice versa, endocrinological derangements have constant functional effects on the nervous system, and probably at times even structural ones. The interrelationship of neurological and endocrinological functional and structural systems is close and warrants a consideration of the psychiatry of endocrinological and cerebral psychopathology at the same time.

The adaptation syndrome can be provoked by both physical and mental stress; it leads to endocrinological, emotional, and neurological sequelae. Even in animals the nervous system is involved together with the endocrine system in the reaction to stress. The nervous influence is even more differentiated and important in man. The new working hypothesis of medicine, in connexion with the discovery of the adaptation syndrome, is in need of a synthesis of the psychopathology of endocrine and cerebral functions.

These examples may suffice to demonstrate the urgent need to consider again the neglected psychiatry of brain diseases. In the near future we should come to definite and generally acknowledged conclusions in regard to fundamental questions, such as: What is the role of the psychopathological findings in the diagnosis of cerebral diseases? What is the psychopathology of acute and chronic, of general and localized, brain lesions? What is the interrelationship of cerebral and endocrinological psychiatry?

I wish to present first some recent research work done at our Zurich Clinic. Then I shall try to formulate a working hypothesis in regard to some fundamental and primary questions of the psychiatry of cerebral diseases.

Psychopathology of Brain Tumours

The first study I want to mention concerns the psychopathology of brain tumours. This study has been carried out by Wanner (1950), Walther (1951), and Blickenstorfer (1951). It is different from many former studies of brain tumours, because they did not look for their cases in psychiatric hospitals; they considered every case which had been admitted to the Zurich Neurosurgical Clinic, quite independently of the presence or absence of any mental derangement. They have made a very thorough personal study of 67 tumour patients, in whom the exact pathology had been established by operation or at necropsy. They studied 600 further tumour patients on the basis of the routine psychiatric examination. Special attention was paid to the premorbid personality. In 121 unselected cases a systematic genealogical investigation was carried out and 1,380 close relatives of the tumour cases were studied. We got for the first time an exact family picture of tumour cases with different psychopathological findings and could compare them with each other and with the family picture of patients with functional psychoses.

Of the 600 tumour patients 70% had psychopathological derangements and 30% were not psychologically altered.

The first interesting finding concerns the fact that most of the psychopathological pictures are very uniform. There is no such variety of clinical pictures as is suggested by a part of the literature. These studies show clearly that the literature has often selected the rare, exceptional, and puzzling psychopathological pictures. The older literature does not sufficiently stress the fact that most tumour patients with mental symptoms—namely, 83%—always display the same two psychopathological syndromes: a *clouding of consciousness* in the acute episodes and an *amnestic syndrome* in the chronic stages.

Clouding of Consciousness and the Amnestic Syndrome

Clouding of consciousness was present at times in 37% of the tumour cases with psychopathological findings. Most frequently we have to deal only with very mild forms. The patients are somewhat sleepy and indifferent, attention cannot be fixed in a normal degree, and mood is frequently changed without psychological reasons. Under stress or in an active stage of the tumour, these mild changes pass over into somnolence, more severe twilight states, delirious states, or coma. As a rule, they revert after a rest to the former condition if the underlying somatic condition is not progressive.

A chronic amnestic syndrome is observed in 38% of the tumour cases with psychopathological findings (the same frequency as the acute alterations of consciousness). "Amnestic syndrome" is, of course, a poor label for the syndrome in question. It is true that the impairment of retention and of memory (involving recent events more than remote ones) are important symptoms. However, the old name gives the impression that amnestic symptoms are the only or the most important ones. This is not the case. The whole personality is impaired, not only the memory and retention. There is damage to the train of thought; the number of ideas on which the patient relies in his arguing becomes scanty; intellectual processes are influenced in too high a degree by moods and impulses; concepts become vague and generalized; or the patient grasps only a single detail of a situation, neglecting other important ones. There is also a tendency to perseveration, to confabulation, and to increased fatigability. The emotions become too labile, and responsive only to what is readily understood. Furthermore, there is a general loss of interest combined with a diminished ability to deal with a variety of ideas and observations.

In its insufficient comprehensiveness, therefore, "amnestic syndrome" is a misnomer; but there is no better generally accepted name. Some schools use the term "Korsakoff syndrome"; but this is confusing, too, because what Korsakoff described 64 years ago is quite another nosological conception. Forty years ago our Clinic called this syndrome "psycho-organic syndrome"; this was at a time when it was not known that many other organically caused psychosyndromes existed. For this reason the term is not a good one. The same is true of the term "chronic organic reaction type." It is regrettable that this organically caused, frequent, and important syndrome, familiar to every psychiatrist, does not have a generally intelligible name. The lack of a generally accepted name contributes to the difficulties in mutual understanding between different psychiatric schools.

Clouding of consciousness in brain-tumour patients—leading in the severe cases to somnolence, delirious states, or to coma—as a syndrome fits into the acute exogenous reaction type of Bonhoeffer or into the acute organic reaction type, as English authors have called it.

It is of the same nature as the cloudiness, somnolence, delirium, and coma in cases of concussion, of brain intoxication, or of severely impaired cerebral blood circulation. It is, on the other hand, quite different in nature from acute schizophrenic, manic-depressive, or hysterical episodes or of other acute mental conditions without organic cerebral derangement.

A similar statement holds true, of course, for the amnestic syndrome: it is no different in chronic tumour cases from what it is in other forms of chronic diffuse cerebral damage, such as chronic alcoholism, other chronic intoxications, the simple form of general paresis, senile and arteriosclerotic dementia, etc. On the other hand, the amnestic syndrome of brain-tumour cases is entirely different in kind from the syndromes in chronic mental diseases without known cerebral pathology, such as, particularly, schizophrenic deterioration or a neurotic personality development. We come to the conclusion that *the psychopathology of the great majority of mental derangements in tumour cases is characteristic of an acute or chronic mental condition of cerebral origin, but is not characteristic of brain tumour as such.* It is similar to mental conditions due to other cerebral diseases.

Neither clouding of consciousness nor the amnestic psychosyndrome is specific for brain lesions of any particular localization. This holds true in our material for brain tumours: both syndromes are found with tumours of all localizations, and the differences in the frequency with which they are shown with tumours of one part of the brain or another are slight and statistically not significant.

We must face the fact, therefore, that clouding of consciousness and the amnestic syndrome, which comprise 83% of the mental alterations due to brain tumour, have no meaning in regard to the locality of the tumour.

Symptomatic Epilepsy and the So-called Frontal Psychosyndrome

What about the remaining psychopathological syndromes in brain-tumour cases?

The third mental condition, much less common than the two just mentioned, is a symptomatic epilepsy. General convulsions or petit mal occurred in 8% of the 600 tumour cases. In regard to epilepsy, our study reveals only what has been known for a long time: epileptic seizures may complicate nearly all brain tumours in almost any site. There is, however, a difference in frequency in different localizations; they are rare in cerebellar tumours and most frequent in the tumours of the parietal and temporal lobes.

A clear-cut so-called frontal psychosyndrome occurred in our material only three times. (It is characterized by a change in impulsiveness and of mood, without real defects of memory or intellect; the impulsiveness can be diminished and dullness can prevail, with slowness of intellectual processes; on the other hand, the mood can be elated, with the tendency to make silly puns and jokes; in any case, there is an impairment of more differentiated interests, of morality, tact, and social responsibility.) In all three cases it was associated, as expected, with a frontal tumour. This small number, however, is not conclusive. In other series of patients I have often found a psychosyndrome similar to the frontal psychosyndrome, although there was no frontal lesion, but brain damage in another locality—for instance, a diencephalic lesion. The so-called frontal syndrome is, according to my experience, not characteristic of a frontal lesion, but occurs also in most other brain lesions if they are localized.

The uncinate fits and dreamy states described by Jackson seem to be more reliable regarding localization. They occurred 17 times among our 600 tumour cases, mostly with temporal localization; but we have also observed characteristic fits and dreamy states in one case of frontal tumour. The most reliable localizing sign seems to be real sleeping spells (which have to be clearly distinguished from mere sleepiness). They occurred six times in our material; in each case the tumour had damaged the hypothalamus or the brain stem in its neighbourhood.

Symptoms which have a definite localizing significance are, of course, aphasia, apraxia, and agnosia, which occurred in nearly 10% of our patients. They are, however, more of a neurological than a psychological nature.

These observations make it clear that the psychosyndrome in brain tumour is in most cases independent of the locality of the tumour. In less than 5% of the cases—namely, in those with sleeping spells and uncinate fits—has the psychopathology a fairly reliable significance regarding localization. Epileptic fits and the so-called frontal psychosyndrome give a hint, but only an unreliable one.

Non-organic Syndromes

Symptoms of a non-organic nature—schizophrenic, manic-depressive, hysterical, or neurotic pictures—are very rare in tumour cases, apart from those which have been selected from mental hospitals. They occurred in less than 5% of our material. In this respect the literature, which describes depressions or so-called symptomatic schizophrenia and other seemingly functional states in brain tumours, is unrepresentative.

The small number of non-organic syndromes in our material of unselected brain tumours demonstrates that our present psychopathological knowledge is exact enough to differentiate in a great number of cases troubles of neuropathological origin from those without neuropathology. But what is the nature of the rare schizophrenic or manic-depressive pictures in brain tumours? A study of genetics has answered this question. Among the relatives of tumour cases with schizophrenic symptomatology are many more schizophrenics and schizoids than in the average population; and, likewise, among the relatives of tumour cases with manic or depressive symptomatology are many more manic or depressive patients. It will also often be found that tumour patients with schizophrenic or depressive symptomatology displayed schizophrenic or depressive episodes long before a brain tumour developed. The families of tumour patients with cloudiness or with the amnestic syndrome, on the other hand, have exactly the same incidence of psychoses as the average population.

The genetic studies therefore reveal two facts: the brain tumour does not cause manic-depressive or schizophrenic reactions, but clear-cut organic reactions; it may, however, be complicated by schizophrenic or depressive reactions which have to a large degree other than neurological causes.

We further considered why cloudiness or the amnestic syndrome occurs in more than half of the tumour cases

but not in the remainder. With regard to the cloudy states, these are closely connected with the speed of growth of the tumour, with intracranial pressure, and with the general physical condition of the patient. This statement is much less true for the amnestic syndrome. The frequency of that syndrome was found to depend mostly on the patient's age. The amnestic syndrome never occurred in tumour cases in children and in adolescents under 20 years; and in patients aged 20–40 it occurred in only 3.5%. On the other hand, it occurred in 36% of the cases in the age group 40–60 and in 57% of the cases over 70.

Some Questions and Answers

The present state of our knowledge of the psychiatry of brain tumours permits of definite answers to definite questions from the neurosurgeon.

1. What is the meaning of the psychopathological findings regarding diagnosis of brain tumours?—*Answer:* They permit, if present, of a fairly certain diagnosis of the presence of an abnormal process in the brain, but do not help to answer the question whether this brain process is a tumour or not.

2. Do the psychopathological findings permit diagnostic conclusions to be made regarding the locality of a brain tumour?—*Answer:* As a rule they do not; in only a very small minority of cases may the psychopathological findings give an uncertain hint of its locality.

3. Do the psychological findings allow diagnostic conclusions to be made regarding the intracranial pressure?—*Answer:* Cloudiness, twilight states, somnolence, and coma are fairly regular sequelae of increasing or very high intracranial pressure; the same mental conditions, however, might also be caused by other complications of the brain tumour, such as general cachexia, circulatory disturbances, etc.

4. What is the diagnostic meaning of schizophrenic, manic-depressive, or neurotic pictures without psychoorganic features in suspected or certain brain tumours?—*Answer:* They are highly dependent upon non-cerebral causes, and allow no diagnostic conclusions to be made in regard to the existence, the locality, or the nature of a brain tumour.

Objections can be made against any attempt to draw more general conclusions. It is hard to decide, for instance, whether the mental symptoms in a tumour case are due to the localized damage, to the effect of the tumour on the circulation, to the water metabolism of the whole brain, or to the intracranial pressure. We greatly need to study many varied cerebral diseases of another kind. In our clinic we have particularly studied Friedreich's disease, myotonic dystrophy, chronic cerebral intoxications, cerebral forms of leukaemic diseases, and different pituitary diseases. We have also tried to arrive at a survey of the very wide literature. Recent experience of psychosurgery, the knowledge of which has been so wonderfully elucidated by English authors, plays a particularly important part.

Psychopathology of Cerebral Disease

What are the factors which determine the psychopathological picture of any cerebral disease? There have to be considered the quality, the extent, the locality, and the speed of the cerebral disease; the physiological functions involved, like the circulation, the pressure, the metabolism; then the constitution and the momentary disposition as well as the psychodynamic development of the patient. Some of these factors have been overemphasized for long periods, while others were neglected.

The quality of the somatic process has been overemphasized by many older psychiatric schools. They believed in well-circumscribed disease entities. It was thought that a specific kind of damage (for instance, a specific infection) leads to a specific somatic lesion which is accompanied by a specific psychopathological picture. Such a conception goes back to the old French school of Pinel and Esquirol, who were greatly influenced by Linnaeus's *Systema Naturae*. As Linnaeus had succeeded in grouping the plants and animals in species, an attempt was made to group psychopathological phenomena in definite disease entities. The nosology of Kraepelin was based on such a speculative conception.

We nowadays ought to realize that there are no specific disease entities and no combinations of specific symptoms with specific pathological processes. Senile dementia may show exactly the same psychopathology as an alcoholic deterioration, a simple form of general paresis, a post-commotional state, or a leukaemic disease with cerebral damage in an older man. The psychopathology of delirium tremens, which has been spoken of as a specific alcoholic psychosis, can be found in exactly the same form in a delirium caused, for instance, by psychotonic amines. I have observed it both in mescaline and in methylamphetamine intoxication. The so-called classic picture of general paresis is by no means characteristic of luetic encephalitis, as was believed by two or three generations of psychiatrists.

Everyone agrees to-day that other forms of general paresis, which are no more specific in their psychopathology, are much more frequent in general paresis than the classic manic form. Though less often mentioned, the contrary is also true: nowadays, as general paresis has become rarer, a great number of the cases with the typical textbook psychopathology of the manic general paresis are not due to general paresis. We have found a so-called paretic symptomatology in brain tumours, in Huntington's disease, in cerebral arteriosclerosis, etc. In our clinic more than half of the cases with a classic mental picture of manic general paresis have no paresis. It would be easy to give further examples demonstrating that it is time to drop the old belief in the existence of mental disease entities which regularly and exclusively accompany one specific physical disease. Each time, however, that a new pathological cerebral process becomes known much work is done in vain to determine a specific psychopathology. This was true, for instance, when the cerebral forms of Buerger's disease were described.

The speed factor has always been recognized as very important in the psychopathology of a cerebral process. Since the time of Bonhoeffer a distinction has been made between the acute and the chronic organic (or exogenous) reaction types. The difference is indeed obvious. In the more severe acute organic reaction types consciousness is affected and somnolence, coma, and delirious and cloudy states are frequent. The different amnestic symptoms, as observed in the chronic reaction types, also often appear in the acute types; but they are very varied in degree, coming and disappearing, and show even less correlation between each other than in the chronic states. In some cases, however, an acute Korsakoff psychosis (as caused, for instance, by a brain contusion) might be very similar in its manifestations

to a chronic Korsakoff psychosis. I have nothing essential to add to the well-known distinction between acute and chronic organic reaction types.

I would point out, however, that on the basis of our modern knowledge the influence of the localization of a brain lesion on the psychopathological picture should be considered in a somewhat different way from what is usual. There has been a tendency to underestimate the importance of the simple distinction between a diffuse brain process and a strictly localized one; on the other hand, the tendency to correlate a specific psychopathology with the exact localization of a brain lesion has certainly been overstressed.

Diffuse Brain Lesions

We still do not know for certain whether the different symptoms of the amnestic syndrome have anything to do with localization in the brain. There is much evidence that the amnestic syndrome generally is the expression of a very diffuse brain damage and has not much connexion with any particular localization.

We find diffuse brain damage in nearly all cases of amnestic psychosyndrome, and vice versa. I never could be convinced by such theories as those of Gamper and Gruenthal, who attribute the amnestic syndrome to a lesion of the corpora mammillaria. I think that the anatomical evidence is far from proving any dependence of the amnestic syndrome on a localized lesion. I also feel that the newer approaches to psychopathology have demonstrated that the amnestic syndrome is produced by an alteration of the whole personality in the sense of the *Gestalt* psychology and not by a sum of independent symptoms. It might seem to be possible to explain a single symptom such as a memory defect by a localized defect. It is hard to conceive, on the other hand, that such a general deterioration affecting the whole intellectual and emotional life and every single psychological reaction should be due to circumscribed brain damage extending over such a small area. Henri Ey has recently pointed out how much both the pathological and the psychological knowledge of modern times make it probable that the general personality deterioration which is seen in the amnestic syndrome is a sequel to damage to brain function as a whole. Our knowledge is not sufficient to formulate definite laws, but the present working hypothesis *should regard the amnestic syndrome as the manifestation of a diffuse chronic brain process.*

So far as we know, the psychopathological results of *circumscribed cerebral lesions* differ very much from those of diffuse brain lesions; they lead to alteration of the emotional response, to apathy, or to general irritability; they also can extinguish or strengthen one or another impulse, instinct, or interest, such as hunger, thirst, sexuality, aggressiveness, etc. They disturb the harmony between the different instincts; there are, for instance, quite often sudden uncontrolled moods or impulses which dominate the whole personality for a short while. On the other hand, there are no amnestic symptoms in localized brain diseases, and the patient's powers of judgment seem to be disturbed only by the emotional changes and not by primary intellectual damage.

Three Fundamental Reaction Types

We have therefore to deal with three fundamental reaction types to cerebral diseases: (1) the acute organic or exogenous reaction type; (2) the amnestic reaction type or the psychopathology of diffuse chronic cerebral lesion; and (3) the reaction type to chronic localized cerebral lesion.

The reason why the conception of a somewhat uniform type of reaction to chronic localized cerebral lesions has not been acknowledged in its diagnostic and theoretical importance is evident: for decades it was assumed that disease in a specific locality of the brain caused a specific psychopathology. It is amusing to study historically how the concepts of a frontal, a diencephalic, a temporal, etc., psychopathology were formed. The frontal psychosyndrome, for instance, was not named in this way on the basis of observations demonstrating that it is different from the psychosyndrome of brain-stem lesions. On the contrary, the psychopathology of frontal lesions was described on the speculative assumption that it had to be quite different from the psychopathology of any other localized brain lesion.

It is much more difficult to separate different psychosyndromes in different brain localizations than to separate different neurological syndromes. If we compare the two main psychosyndromes of local cerebral lesions—the frontal and the stem syndrome—we realize how similar they are and how difficult it is to distinguish them. Both lead to changes of emotions, of mood, of impulses and instinct, and any psychic symptom of the one can also be found in the other. It may be true that the identification of the frontal patient with his emotional changes goes much further than in the brain-stem patient. The frontal patient will often find his mental state quite natural, and is inclined to blame the environment and not his disease for his social difficulties; the post-encephalitic patient, on the other hand, frequently realizes that he is under a morbid influence which is alien to his original personality, and he might call his emotional symptoms morbid and even compulsive. But nobody would dare to give a differential diagnosis of frontal or brain-stem lesions on the basis of the subjective attitude to the mental changes.

There is a common frame into which all the psychosyndromes observed in chronic localized brain lesions fit very well. Their similarities are more important than their dissimilarities, so far as they are known to-day. The existence of different psychosyndromes in different localized brain lesions can be overstressed; and it is well to work with the conception of one psychosyndrome in localized chronic brain lesions of any kind.

Even within the three fundamental syndromes of organic reaction types there are marked differences from case to case. To what are they due? There is much evidence to show that they depend to a large degree on the personal constitution. The family pictures of organic reaction types with schizophrenic or affective or neurotic colouring are statistically proved to be similar to the family pictures of schizophrenic, affective, or neurotic patients. We also found very interesting examples which demonstrated the pathoplastic influence of constitution: we found, for instance, extremely similar psychoses in brain tumour of quite different localization in siblings. Other studies concern the psychodynamics of organic reactions. If one knows thoroughly the personality of organic mental patients—formerly a matter of little interest—one will be excited to find how clearly the personality, with its conscious and unconscious impulses and fears and wishes, is projected in the morbid symptomatology.

The Age Factor

Another factor with an important influence on the organic psychopathology, and one which has been much neglected, is the age of the patient. I have mentioned before that in tumour cases memory for the recent past is much more often damaged in old than in young age groups. We studied the influence of age on the frequency of the amnestic syndromes also in other diseases, such as intoxications, head injuries, epilepsy, Friedreich's disease, and so on, and came to similar conclusions. Lutz, the chief of our children's department, has followed the question in children. Amnestic syndromes are extremely rare in children. If the child's memory is affected, for instance after a head injury, the impairment concerns the remote memory and not retention and recent memory. It looks as if a diffuse brain damage just increased the physiological peculiarities of memory. In the child the memory for remote events is normally very poor, while for the recent ones it is excellent.

Brain damage exaggerates this difference. The opposite is true for older people. Age, however, is not the only factor which influences the frequency of the amnestic syndrome. There are rare cases of severe brain damage in old people without the amnestic syndrome and even rarer cases of the syndrome in childhood. There must be factors in the genesis of the amnestic syndrome which are still unknown.

Summarizing a working hypothesis in regard to the present state of organic psychiatry, I should therefore point out that we cannot believe any longer in the conception of Kraepelin and the old French schools, which tried to discover specific psychopathologies for special brain lesions. We cannot explain the mental symptomatology of cerebral diseases by considering their locality alone, as Gall, Meynert, Wernicke, and, later, Kleist tried to do. So far as is known, the psychopathology of cerebral disease is dependent to a large extent on (1) whether the brain disease is of a chronic or an acute nature; and (2) whether it affects the whole brain or a part of it. It is reasonable to distinguish three large psychopathological patterns or psychosyndromes: the acute organic syndrome, the chronic psychosyndrome due to a diffuse cerebral lesion, and the chronic psychosyndrome due to a localized cerebral lesion. The psychopathology of brain disease is further influenced by the age of the patient, his constitutional background, and his psychodynamics.

Such a conception not only seems to simplify the description of organic pathology but it is also useful in diagnosis and gives some hints for therapeutic research. It points out, for instance, that study of localization may perhaps be not the only research approach for further progress in psychosurgery. It seems to me that we are also much in need of studies on the extent to which the results of psychosurgery depend upon individual constitution and psychodynamic factors.

Endocrine Psychodynamics

For ten years now the endocrine psychosyndromes have been the favourite field of my personal research. The mental pictures of endocrine diseases depend much less upon the kind of gland affected than is generally supposed. It is true, of course, that many specific endocrine lesions have fairly regular emotional sequelae; as a rule, the sexual impulse is diminished by castration, and general activity is increased in hyperthyroidism and diminished in hypothyroidism, etc. However, even these rules are not without frequent exceptions. Many English authors, for instance, have stressed that hypothyroidism may be accompanied by other than the usual hypothyroid mental symptoms; hyperthyroidism may cause stupor, and castration may not diminish the sexual impulse, etc.

In pituitary and adrenocortical diseases the lack of coordination of the physical disease and its mental symptomatology is quite striking. The psychopathology of acromegaly and that of Cushing's disease are in many ways similar. It is even more surprising that the psychopathology of Cushing's syndrome and that of Addison's disease are by no means contradictory, but rather similar. In short, we have to deal with a similar independence of the psychosymptomatology of the localization in both endocrine and cerebral disease. In both cases constitution, psychodynamics, and other factors have an important influence on the psychopathology.

The general pattern of the chronic endocrine psychosyndromes is identical with that of the chronic psychosyndromes in localized cerebral lesions. As a matter of fact, there hardly exists any endocrine mental syndrome which cannot be observed also as a sequel to a localized brain lesion, and vice versa. This fact is in complete harmony with the common physiological knowledge that the endocrinological and nervous functions are dependent on each other. Parts of the endocrine system and parts of the nervous system form functional units. The final psychological effect is the same, whether such a functional unit is damaged in its endocrine or in its nervous aspects. It even seems to happen often that a lesion in the nervous system leads to a functional or even anatomical lesion in the endocrine system, and vice versa.

I feel that the knowledge of the interrelationship of psychosyndromes of endocrine origin and those of localized cerebral origin may give rise to interesting speculations. Psychosurgery may have resemblances to endocrine therapy. It is indeed curious to note how much, for instance, the development of an acromegaly is accompanied by exactly the same mental changes as those we observe in some patients after leucotomy. Surgery of the brain may in some cases be replaced by intervention at the endocrine level.

There is yet another aspect of the facts I have mentioned: a close interrelationship between emotional stress situations and endocrine functions. This has been known for a long time to hold true for Graves's disease, for instance, and has been displayed from a new angle by the doctrine of the adaptation syndrome. It seems, however, that endocrine changes lead to functional and structural nervous changes, and vice versa. The knowledge of the close interrelationship of cerebral and endocrine mental syndromes opens wide vistas in psychosomatic medicine. Endocrine function seems to be a bridge between the psychological stress situations and definite circumscribed cerebral functions and structures. Those considerations are, of course, still mere speculations, which might lead to illusions. They demonstrate, however, the interest which further clinical study of the psychopathology of organic diseases deserves.

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SOCIAL ADJUSTMENT OF NEUROTIC PATIENTS AFTER PREFRONTAL LEUCOTOMY

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In this paper the results of a follow-up into the social adjustment of 30 neurotic patients treated by bilateral prefrontal leucotomy are discussed. The length of time since operation varies between eighteen months and eight years, the majority having been observed for three years or more. Many cases had a relatively unsettled period, usually for about six months, after operation, while others, apparently well on leaving hospital or for some months afterwards, have later shown defects in their adjustment. For this reason the early course after operation has been excluded from discussion, and the patients in this follow-up have all now arrived at a relatively stable social level.

These patients were all operated upon by the same surgeon, Mr. Wylie McKissock, whose technique has been described elsewhere (Fleming and McKissock, 1943), while the cut in all these cases was purposely made relatively more anterior than that usually used for psychotic cases.

No patients were included in this series if their illness had at any time shown psychotic features, while those cases which were diagnosed as psychotic depressions, whether endogenous or exogenous, have also been excluded.

All cases had been under observation for at least several months before operation and an assessment made by more than one psychiatrist, and only those in which there was agreement on the neurotic nature of the illness have been included.

The patients were followed up by out-patient consultations, often with the psychiatrist who originally treated the patient in hospital. They were also, for the purpose of this paper, interviewed at home, and their relatives and employers were visited, all by the same social worker. Some of the cases were under our own care, but most were under the care of colleagues. Of the neurotic patients passing through the hospital in the eight years concerned only one in 300 was leucotomized.

The type of neurotic patient who was selected for operation always showed the following features. (1) The previous personality had considerable drive, and, in particular, the patients had made an attempt to continue their way of life even with severe symptoms. (2) All the illnesses had marked tension as a presenting symptom. (3) No other treatment was thought likely to give relief; in practice, other methods of treatment had already been tried and had failed to give lasting relief. (4) All, at the time of operation, were considered to be incapable of living their lives outside hospital unless they had relief from their illness. Cases were rejected which had antisocial or overt aggressive tendencies in their histories, as were recurrent depressives with marked mood swings.

Although the diagnoses could be grouped under the headings of anxiety states, depressions, and obsessive-compulsive neuroses, in fact most cases had features of all these reaction types. For example, several patients had originally attended a psychiatrist for mild anxiety symptoms. A year or two later it was noted that some depression was also present. Later still, obsessional symptoms occurred, until by the time operation was considered the clinical picture showed all three components. All the cases of obsessional neurosis had well-marked depression secondary to their obsessional illness. It may be said that these patients are those whose nervous systems were able to develop and withstand marked mental tension over a long period, the average duration of illness in this series being eight years.

Literature

Most previous reports have been concerned with results of operation on psychotic patients. The Board of Control (1946) showed that obsessional neuroses made a relatively good recovery. Roughly 55% were "citizens" after operation, compared with 40% manic-depressives and 16% schizophrenics. Watts and Freeman (1944) reported on a series of obsessive tension states and recorded that 67% were afterwards leading useful lives. They considered that their patients showed no significant intellectual or emotional impairment, and that they made a better practical use of their intelligence after operation. The findings in the present series do not support these optimistic statements. On the other hand, the report of Ström-Olsen and Tow (1949) suggested that all of their group suffering from neurotic depression, obsessional states, and tense hypochondria suffered from some personality defect. These findings will appear pessimistic compared with the results of this inquiry, but perusal of their case histories suggests that their patients were probably more nearly psychotic than ours.

Partridge (1950) discusses the results in 24 cases of obsessional illness, but otherwise comparison is difficult because all his depressives are considered together and the majority were presumably psychotic. In general his results with obsessional illnesses are in agreement with those of the present series.

Results

In assessing the results, consideration has been given to the previous personality and level of adjustment, as some patients had always been handicapped by personality defects, while others had been normal citizens. Although the patient's own account of his stability and behaviour is of value, it has to be evaluated in the light of the relatives' and employers' statements. Lack of insight into the attitudes of others and lack of self-awareness after leucotomy lead the patients into errors of judgment of their own performance. For example, one obsessive-compulsive insisted that no change had occurred, although observation showed that her rituals now occupied half an hour instead of four hours. On the other hand, many patients state that they are fully recovered and have no complaints, while relatives will point out very clear defects in their behaviour.

As all patients were completely incapacitated at the time of operation and are now out of hospital and living at home, it is clear that some measure of improvement has occurred in all. It can be said that they now suffer less from their illness, and even if not well can be looked

after at home instead of in hospital. It is convenient to grade the results into four levels of social function.

Full Recovery

In the first group are those patients who have made a full recovery. This means that not only are they symptom-free but that after the operation there is no defect which hampers their lives.

A married woman aged 32 had no psychiatric illness in her family and her early life was happy and uneventful. She had been kept ignorant of sexual matters, and her first neurotic breakdown at 18 occurred after a man had exposed himself to her. At this time she had anxiety symptoms with phobias and some depression, from which she made a full recovery without specific treatment. A second breakdown with similar symptoms occurred at 21. This was probably the result of conflict over sexual activities. Convulsion treatment was given without benefit, but she recovered after about three years. She married when 26 and was very happy and had two children. The third breakdown was precipitated by the overseas posting of her husband, who was in the Army. She was admitted as a voluntary patient to another hospital for six months, received E.C.T., which did not relieve her, and returned home. She was readmitted later, but further E.C.T. and the return home of her husband did not effect a recovery. She was eventually admitted to Belmont. She complained of feeling depressed and anxious, and was depersonalized. She was not retarded nor self-accusatory; her appetite was poor and her sleep fitful. She ruminated over thoughts of suicide and insanity in an obsessional manner. The symptoms had become progressively more severe over three years.

Three years after her leucotomy she was symptom-free and stated that she was glad to be alive. She was managing a teashop and guest house, and her marriage was happy even though her husband, still in the Army, was at the time posted away from home. She had plenty of friends, and her social activities included regular card-playing, swimming, and tennis. Whereas before her illness she had been dependent on others, particularly her husband, she was now quite self-reliant. Her mood was stable, she was tactful with customers and staff, and her social adjustment was entirely satisfactory.

Much Improved

The second group comprises those patients who, although very much improved and leading useful lives in the community, have either some persistent symptoms or defects following operation which prevent full enjoyment of life or full participation in it.

A single man aged 30 had a family history of neurotic illness. He himself had always had neurotic traits and a bad work history, with many changes of job and spells of unemployment. He had always felt inferior, was shy, and was unable to mix freely with either sex. Since the age of 21 he had suffered from attacks of anxiety with trembling, giddiness, and nausea. When 22 he was conscripted, but was soon discharged because of his neurosis. He attended a psychiatric out-patient department and received some psychotherapy. He later became engaged, but decided not to marry because of his illness. He was admitted to hospital when 30, when he was noted to be anxious and depressed, with obsessional thoughts of death and occasional feelings of unreality. He stated that he was desperate, and willing to undergo any treatment for relief. E.C.T. increased his anxiety, but abreactive treatment gave temporary relief. After he had made an abortive suicidal attempt leucotomy was decided on. Four years later he was happily married and was said to be very affectionate towards his wife. Since discharge from hospital he had had regular employment for the first time in his life. He was still very shy in company, however, and this limited their social activities. Also, in the home he lacked initiative and left decisions to his wife. She considered he was very much improved by his leucotomy and was quite content with her marriage.

Improved but Seriously Handicapped

The third group consists of those patients who, although improved and usefully occupied in the community, are seriously handicapped by defects.

A married woman aged 67, the oldest patient in the series, had suffered from obsessional ruminations about death and disease since the age of 23. She had a well-marked obsessional personality, and even in her periods of relative freedom from obsessions her rigid outlook hampered her enjoyment of life. Before her admission for leucotomy she had had one previous period in hospital and considerable out-patient treatment. She was well preserved physically, apart from a mild hypertension, and there was no evidence of senile mental deterioration. Because of her obsessional doubts she was depressed and agitated.

Three years after her leucotomy her obsessions, agitation, and depression had left her completely. She seemed quite happy and contented. Inquiry of relatives, however, elicited the fact that incontinence of urine, which began after operation, still persisted, that she had a marked inertia and no interest in any social life, and that "all depth had gone out of her." Although still doing the housework, she showed no interest or enthusiasm for it, and would often just sit in a chair and leave work to accumulate. Her statement, "Before the operation I was very worried about my son and his fiancée—now I don't seem to care who he marries," is an example of her changed attitude.

It seems reasonable to suggest that the elderly patient may be unable to recover from the lesions produced by the operation because of organic restrictions such as arteriosclerotic changes, and because of the rigidity of personality usual in the elderly.

Social Burden

In the fourth group are those patients who, although perhaps less difficult to nurse and more easily tolerated in a home, yet remain a burden to the community.

A spinster aged 24 was an only child. Her mother had a history of emotional instability but no overt breakdown. As a child the patient had several neurotic symptoms. She was a good scholar but always shy, had a quick temper, and since the age of 10 had developed increasingly marked obsessional traits. She had left three jobs because of neurotic symptoms. When 10 years old she began worrying over being fat, and on starting work was slow and always afraid she would do something wrong. From the age of 24 her symptoms had increased, the most severe of them being obsessional doubts. During the year before entering Belmont she had received considerable out-patient psychotherapy and E.C.T. twenty times. On admission she was noted to have marked obsessional ruminations, little depression but considerable anxiety, with palpitation and sweating.

This patient appeared to improve considerably after operation, and follow-up a year later found her at work again and with few symptoms. Five years later, however, she was unemployable, a recluse at home. She had spells of depression and took "herbal treatment." She occupied herself reading or listening to the wireless. Her symptoms were not as bad as before operation; but to her slowness, as a result of her obsession, was added an inertia presumably the result of operation. She was also irritable with her parents, who found her difficult to live with apart from having to support her. Possibly as a result her father was inclined to be "out a great deal on business." She seemed resigned to not feeling well.

The early history of this patient revealed schizoid personality traits: she lacked the warmth and depth of feeling present in the patients who made a good recovery. Another of this "social burden" group also had schizoid traits, and both are now living a restricted life at home. Schizoid traits are thus of bad prognostic significance, as they may be accentuated after operation. It may be

that the relief of tension in those patients with schizoid traits removes the anxious drive and leaves the patient more detached, apathetic, and inert.

The clinical description of the illness and the results obtained are shown in Table I.

TABLE I

	No.	Full Recovery	Much Improved	Improved but Seriously Handicapped	Social Burden
Neurotic depressions	10	3	—	6	1
Obsessional states:					
Largely ruminative	7	3	3	—	1
Largely compulsive	7	2	3	1	1
Anxiety states ..	6	2	3	1	—
Total ..	30	10	9	8	3

Only seven cases have been followed up for less than three years ; two of them are social burdens and two are seriously handicapped. The figures are too small to be significant, and, although they suggest that there is a tendency towards improvement with the passage of time, it is possible that in the last four years less suitable cases have been accepted for operation.

The sex ratio and marital state in this group are given in Table II.

TABLE II

	No.	Full Recovery	Much Improved	Improved but Seriously Handicapped	Social Burden
Male	9	2	3	2	2
Female ..	21	8	6	6	1
Married ..	16 (+5)	6 (+2)	5 (+3)	5	—

Figures in brackets indicate the number who have married since the operation.

It is apparent that the men were not so successful in readjusting as the women, but the figures, of course, are small. Married patients made a relatively good adjustment. This probably affects the social factor in recovery : a married woman returns to an environment where she is " at home " ; a single man has again to find work and perhaps a mate.

Previous treatment included E.C.T. in 22 cases, insulin coma in 5, modified insulin in 10, deep narcosis in 8, abreactive technique in 7, and psychotherapy (of at least three months' duration) in 7.

The results of the treatments were assessed and compared with the result of leucotomy, but were not found to be prognostically significant in any way. This is contrary to the views and findings of others. The analysis of the duration of illness before operation revealed no evidence that this had any influence on the result : neurotics appear to differ from psychotics in this respect.

The influence of the presence of neurotic traits in the personality before illness and of a family history of mental disorder is shown in Table III.

TABLE III

	No.	Full Recovery	Much Improved	Improved but Seriously Handicapped	Social Burden
Previous personality free of neurotic traits	9	3	2	3	1
No family history of psychiatric illness	9	3	2	2	2

Again the numbers are small, but it is interesting that most of those who made a full recovery had neurotic traits and a family history of mental illness, while among those who became social burdens or made a poor recovery were patients who had a normal family and previous personality. The possible significance of this is discussed below.

The influence of age on prognosis is suggested by Table IV.

TABLE IV

	Full Recovery	Much Improved	Improved but Seriously Handicapped	Social Burden
No. of cases ..	10	9	8	3
Average age ..	41·4 years	35·2 years	36·4 years	26·3 years

The five patients under 26 are in the third or fourth category, and of the three patients over 50, one made a full recovery and the other two are improved but with serious social defects. Thus the best results occurred in the middle-aged.

The practical efficiency of the patient either at work or in the domestic sphere was analysed (Table V). It should

TABLE V

	Improved	Static	Worse
Work status (men and single women) ..	4	2	7
Domestic efficiency (married women or single girls caring for patients) ..	4	4	3

be remembered that the comparisons are with the patient's best previous achievement.

The remaining six patients were married women who not only ran a home efficiently but also went out to work. They had all done this before, and their efficiency was essentially unchanged.

Of those male patients whose work had improved, one has the same job but has been given a rise of pay, which he considers is evidence of his increased efficiency, another (a clerical worker) is now in charge of a new department and has increased his prospects of further promotion. The other two are in regular employment of a semi-skilled nature which previously they had been unable to do. Some patients are now able to accept responsibility of which they were previously afraid.

Where the work status has deteriorated the common factor seems to be that the patient now lacks self-criticism and ambition, so that he tolerates a low standard of production, does not look for a better job, and has no desire for responsibility.

Personality Changes

This series of patients reveals contrasting changes in personality. Previous reports have suggested that a " leucotomy syndrome " of personality change can be found, often socially undesirable in that apathy, carelessness, and lack of regard for convention form part of it. Other writers have suggested that there is usually a change for the better : their patients are described as more sociable, having a greater self-confidence and a more practical approach to life. This follow-up has revealed no constant pattern of change either of improvement or of deterioration. For any change in personality one observes in one patient, the opposite can be found in another. For example, some patients are more

friendly and sociable, others more retiring; some are more garrulous, others quieter; some are more happy-go-lucky, others more careful and persistent. What is more, both kinds of personality changes can occur with benefit to the patients concerned, depending on their social *milieu*. For example, a more care-free attitude towards work may develop in an obsessional patient with benefit to his actual performance, while an anxious patient previously careless at work because of his emotional state may become a more careful and persistent worker after leucotomy. In the case of one patient whose tensions often provoked quarrels at home, the reduction of tension and subsequent calmer behaviour were welcomed by all the relatives. On the other hand, a previously restrained and timid woman who had broken down under the stress of a psychopathic family became much more quick-tempered and outspoken than before and kept her family in order, again to their admitted benefit. The personality changes that follow leucotomy depend on the previous personality and which aspects of behaviour have been either promoted or inhibited by the tensions, fears, or anxiety of the patient.

Social Defects

These were present in 20 patients, most occurring only in two or three.

Lethargy of sufficient degree to be a social handicap was still present in a third of the patients. It was noted as leading to late rising and early bedtime habits, and an inability to keep up with more active friends, or to plan and execute entertainment at home. The lethargy seemed most marked in initiating activities, as, once started, the leucotomized patient seemed able to maintain a good performance.

Irritability.—One-fifth of the patients were irritable, but no actual violence has been recorded. The impression is gained that irritability becomes less the longer the time since operation; thus it may be an irritative phenomenon as suggested by other writers.

Outspokenness and Volubility.—These are listed together because they often occur together. They do not necessarily occur in patients with irritability; for example, one placid and friendly young woman found that she tended to express her opinion of people quite freely "before I had time to check it." Volubility is often pronounced, the patient pouring forth a stream of conversation which, although coherent, can nevertheless be very trying to the audience. Fortunately such patients do not seem to mind being interrupted.

Less Sociable.—Several patients were less sociable; this trait was so marked in some cases that the whole social life of their family was handicapped. Decrease in sociability occurred in those patients who had previously been sociable in order to fulfil their sense of duty, or whose tensions had driven them out to try to find distraction from their inner fears.

Lack of Feeling for Others.—This was not complained of by the patients but by their relatives. In the three cases in which this was noted the relatives had felt that the good will and coherence of the family were affected by it. As one complained, "She just goes her own way now."

Easily Satisfied and Lack of Ambition.—These two defects were found together. They were obviously more noticeable in male patients for the reason that this particular attitude is prejudicial to success at work. Typical comments were, "He doesn't mind just doing the same job though it's boy's work really"; "He is quite happy as a workman—doesn't try to get a more responsible job"; or, "He doesn't seem to care if he does make mistakes at work now—he's lucky to have an understanding boss." Carelessness at work or in the home also comes from this easily satisfied attitude.

Social Gains

Sixteen patients recorded material improvement in their personality in one sphere or another. Some patients, of course, had improvement in one sphere, defects in another. The improvement was usually the result of the decline in emotional tension which in some way had previously handicapped the patient. It will be noted that several of the improvements are the reverse of the defects previously described—which makes it difficult to accept the "post-leucotomy syndrome" as a single entity. The main social gains are:

Increased Sociability.—Patients found they were less tense in social gatherings and therefore could enjoy company previously shunned. Several compulsive obsessives no longer needed to perform an extensive ritual after meeting people, so that a social life once more became possible. Two patients with anxiety states found themselves able to mix freely without embarrassment for the first time in their lives. In some cases this sociability was of a superficial nature, but in others real gains have occurred.

Self-confidence.—This affects social ease, but is also noted in patients who now rely on their own judgment instead of on others, or who are now active participants in family life rather than parasites on the energies of others.

More Lively.—This again contradicts the idea of universal post-leucotomy apathy. It was noted most in previously shy and inhibited patients (but not schizoid), who now became more active members of their social group. A similar improvement also occurred in some of the ruminating obsessional patients.

More "Practical."—Freeman and Watts considered that the leucotomized patient made a better practical use of his intelligence. This was recorded in only three of the patients in this series, all of them housewives.

Married.—Five patients—one man and four women—have married since operation. In all cases this reflects a real improvement in adaptation to the opposite sex, as all the marriages seem to be successful, although one is under considerable stress owing to the husband's Army service.

It is worth noting that no instance of promiscuity has been recorded since leucotomy, even in cases in which it was present before.

Discussion

The number of patients in this series is too small for the results to be considered more than suggestive. However, compared with other series, it is apparent that patients with neurotic illness respond well to leucotomy. None can be considered worse, while in roughly two-thirds of the cases a severe and crippling illness has been strikingly relieved and the patient enabled to fulfil the role of a useful citizen once more.

Of the diagnostic categories the depressive illnesses have been the least successful. As most neurotic illnesses present a mixture of symptoms, it is possible that this only means that a personality with less underlying drive will present more as a depression than as an anxiety state.

In this series the younger patients made the worst adjustment, irrespective of previous diagnosis. No patient of 25 or under made a good recovery. The best results were achieved in patients aged 30 to 50. It was noted that most had come from unstable families and had experienced lifelong neurotic traits. It is suggested that the neurotic patient who makes a good recovery after leucotomy is often the one who has carried on his or her life in spite of personality difficulties and has broken down in middle age only after repeated stresses. The younger patients who broke down under

the stress of adolescence or early adult life lacked the stamina to make a good adjustment after operation.

Another conclusion is that neurotic patients do not necessarily show the so-called post-leucotomy syndrome. Some are more lively, others more apathetic; some more careful, others careless; some irritable, others calmer. Moreover, these varying traits occur in patients with both good and poor results, and can be evaluated only against the past and present personality and social background. It is possible that the serious personality defects described following operation will be separable into those due to persistence of previous personality defects or disease symptoms, and those due to the cut being made too far posteriorly or in other anatomically undesirable areas.

Summary

A follow-up was made of 30 neurotic patients who had been treated by prefrontal leucotomy. Two-thirds were found socially well adjusted or with minor defects only. The factors on which the result depends are assessed and discussed.

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SIMPLE GASTRIC ULCER AND CARCINOMA

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The possibility that a chronic gastric ulcer may become malignant has excited controversy for more than a century. In the early years of gastric surgery it was commonly believed that a large proportion of gastric carcinomata had their origin in chronic simple ulcers. For example, Wilson and MacCarty (1909) concluded that 71% arose in this manner, and, in this country, Moynihan (1906) stated that about 60% of cases of gastric carcinoma gave a history suggesting previous simple ulcer.

A more moderate school still holds the view that malignant transformation of simple ulcer may occur, but far less commonly. Ewing (1918) concluded that not more than 5% of simple ulcers undergo malignant change, and similar views have been put forward by Dible (1924), Cabot and Adie (1925), Stewart (1929, 1931), and Newcomb (1932). This school bases its opinion largely on the results of pathological studies of post-mortem material and specimens removed at operation.

By contrast, Brown (1930) studied the fate of 1,130 patients in whom there was good evidence of chronic gastric or duodenal ulcer and who were treated medically. In the 77 cases of chronic gastric ulcer only one subsequently developed a gastric carcinoma, and that at a different site from the ulcer. Of the remaining 1,053 patients with duodenal or combined duodenal and gastric ulcer, nine subsequently developed gastric carcinoma. He therefore concluded that chronic gastric ulcer is not a predisposing cause of carcinoma.

The problem is of considerable practical importance because the treatment of gastric ulcer must depend upon which view is held. In making a survey of 375 patients treated in the Radcliffe Infirmary for gastric carcinoma, we were interested to find 26 patients in whom there was some evidence that the neoplasm might have originated in a chronic gastric ulcer. It is our purpose to present the evidence derived from these cases and to discuss it.

Results

In Table III we have set out the salient features of all the cases in which there was evidence that the carcinoma might have arisen from a chronic gastric ulcer. In the final column we summarize the evidence which seems to support this view.

All the cases except two had pathological evidence in favour of their being "ulcer-cancers." We are not competent to judge whether the criteria adopted by the pathologists were adequate to permit of such a diagnosis. The fact that well-trained pathologists came to this conclusion indicates to our satisfaction that the lesions presented the characteristics of peptic ulceration in almost all cases.

If we consider other features of the group of cases, some interesting facts emerge. Only 13 of the patients had clinical histories which we can accept as probably indicating the presence of a chronic ulcer. The site of the carcinoma is also of interest. Of the 26 cases no fewer than 18 were pre-pyloric, the remaining 8 being in the body of the stomach (Table I). This distribution corresponds with what we have found for the site of carcinoma in the whole series of 375 patients, of whom the present group is a sample. It contrasts sharply with the well-known predilection for the body of the stomach shown by chronic gastric ulcer.

TABLE I.—*Site of Carcinoma in Relation to Clinical History of Chronic Gastric Ulcer*

Clinical History of Chronic Gastric Ulcer	Site of Carcinoma		
	Pre-pyloric	Body Other Than Lesser Curve	Lesser Curve
Positive	7*	3	3
Negative	11†	0	2
Total	18	3	5

* Two had separate gastric ulcers on lesser curve.
† One had separate gastric ulcer on lesser curve.

Among the 18 patients with pre-pyloric carcinomata 3 had chronic gastric ulcers on the lesser curve which were separate from them.

It is also of interest to observe the results of the fractional test meal in the 21 patients of this group in whom it was carried out and to compare the results with remaining cases of the parent series (Table II). The present groups showed a much higher proportion of patients with normal or increased free hydrochloric acid.

TABLE II.—*Fractional Test Meal Findings*

	No. of Patients	Normal or Hyperacid	%
Present group	21	12	57·1
Remainder of parent series	162	36	22·2

TABLE III.—*Evidence in 26 Cases in which there was some Evidence of "Ulcer-Cancer"*

Case No.	Age and Sex	Date of Admission	Clinical History	*X*-ray Findings	Operation	Morbid Anatomy and Histology	Diagnostic Criteria
1	46 M.	16/10/47	15 years' epigastric pain, unrelated to meals but relieved by alkalis. Remissions of 6–12 months. 1 year's alteration in character of pain	Large ulcer crater on lesser curve, with rigidity above and below—probably neoplasm	Large shallow ulcer of lesser curve with marked induration	Adenocarcinoma arising in chronic ulcer	History. *X*-ray. Histology
2	61 M.	24/9/48	20 years' indigestion 3–4 hours after meals. 1937: gastro-enterostomy. 1944: barium meal showed G.U. low down on lesser curve. Good response to medical treatment. Intermittent dyspepsia, but 3 months before admission the character of dyspepsia changed	1944: gastric ulcer low down on lesser curve 1948: fairly large ulcer crater low down on lesser curve	Large chronic gastric ulcer on lesser curve	Adenocarcinoma arising in a chronic ulcer. Lymph nodes not involved	History. *X*-ray. Histology
3	66 F.	30/9/46	1934: onset of intermittent dyspepsia 1–2 hours after meals and relieved by alkalis. 1943: anorexia. 1944: admitted because of loss of weight and lassitude. Gastroscopy: small ulcer on posterior wall, well above pyloric region; no evidence of malignancy. Improved with medical treatment. 1946: admitted with 7 weeks' history of anorexia, epigastric pain, and vomiting	1944: Large ulcer crater on posterior wall. Repeat examination in 1944: ulcer smaller on medical treatment		Macroscopic: carcinomatous ulcer arising from the edge of an old scar. Secondaries in the liver. Histology: adenocarcinoma	History. *X*-ray. Histology
4	42 F.	8/7/47	1943: central abdominal pain and vomiting in afternoon for 3 months. 1945: return of pain 3–4 hours after meals; improved with dieting and had periods of freedom up to 2 months. At time of admission no recent change apart from a haematemesis	1945: large G.U. on posterior wall at angulus. 1947: large ulcer at angulus probably fixed	Very large indurated ulcer at incisura, fixed to pancreas	Chronic G.U. with carcinomatous change	History. *X*-ray. Histology
5	55 M.	23/4/40	12 years' epigastric pain with remissions. April, 1939: perforation of gastric ulcer, treated surgically by closure of perforation. Thereafter free of symptoms. Recurrence of pain with radiation to back and bulky vomits for 4 months before admission	April, 1940: pyloric stenosis, probably due to carcinoma	Large ulcer on lesser curve near pylorus. One or two nodules in peritoneum. Very suggestive of neoplasm. Local enlarged glands	Pre-pyloric ulcer. Naked eye suggests chronic peptic ulcer, but histological appearances do not entirely confirm this. Lymph nodes involved	History. Histology
6	53 M.	29/6/43	1917: onset of epigastric pain after meals; relieved by vomiting and by alkalis. No recent change in symptoms	June, 1943: pre-pyloric deformity and deformed duodenal cap	Pre-pyloric carcinoma with many lymph nodes	Ulcer on lesser curve of pre-pyloric region, with thickened edges. Adenocarcinoma arising in a chronic ulcer. Lymph nodes *not* involved	History. Histology
7	51 M.	12/9/41	6 years' intermittent epigastric pain 2–3 hours after meals, relieved by food and vomiting. 5 weeks before admission the pain became continuous, with vomiting and anorexia	1939: barium meal normal. 1941: ulcer crater at angulus — nature unknown	Ulcerated mass on lesser curve	Irregular ulcer not suggestive of malignancy. Histologically an ulcer-cancer	History. Histology
8	62 F.	2/1/40	4 years' epigastric pain immediately after meals, at first with remissions, later continuous. Pain aggravated by food	Large pyloric neoplasm	Large growth adherent to pancreas	Pre-pyloric chronic gastric ulcer undergoing malignant change	History. Histology
9	62 F.	30/11/42	5 years' epigastric pain 2 hours after meals, relieved by food and alkalis, with remissions. Attacks of pain gradually became more severe	Large filling defect of body and stomach	Large mass on greater curvature	Carcinomatous ulcer with an area of scarring proximal to it. Microscopical appearances suggest an ulcer crater	History. Histology
10	50 F.	5/5/39	7 years' dull abdominal ache related to meals with complete remissions. Relief by vomiting and alkalis. Three months' bulky vomits; haematemesis led to admission	Pyloric stenosis, probably simple	Hard, nodular pyloric swelling, with local glands	Deep pre-pyloric ulcer. Carcinoma developing in the edges of a chronic ulcer. Lymph nodes involved	History. Histology
11	73 F.	5/2/48	1905: onset of intermittent dyspepsia. 1927: wedge-resection of G.U. 1929: gastro-enterostomy. Following this, intermittent dyspepsia, when the pain became more continuous and went through to the back	Extensive filling defect of lower third of stomach	Large growth of stomach distal to stoma of gastro-enterostomy. Secondaries in liver and local glands		Histcry
12	41 M.	6/12/46	1943: dyspepsia 2 hours after meals relieved by alkalis and food with periods of freedom. Loss of weight	1944: G.U. low down on lesser curve	Mobile carcinoma of pylorus, with local glands	Ulcer on posterior surface on pre-pyloric region with raised edge. Probable ulcer-cancer. 2–4 lymph nodes involved	Histology
13	36 M.	20/9/40	2½ years previously: isolated vomiting attack. 6 months later epigastric pain 2½ hours after meals with occasional vomiting. 8 months before admission: increased severity of symptoms	Pre-pyloric ulcer and infiltration	Diffuse thickening on lesser curve near pylorus. Small local glands	Pre-pyloric peptic ulcer undergoing malignant change	Histology
14	80 M.	1/4/47	2 years' flatulence. 6 months' epigastric pain unrelated to meals, relieved by alkalis. March, 1947, admitted to R.I. Sent out. Readmitted 1/4/47 with increasing pain	March, 1947: huge ulcer crater on posterior wall near angulus	Posterior ulcer at pylorus— ? malignant	Died 26/5/47 of coronary thrombosis. Chronic G.U. with infiltrating anaplastic adenocarcinoma. Secondaries in glands and lungs	Histology
15	65 M.	2/4/48	2 weeks' epigastric pain 2 hours after meals. 1 week before admission: haematemesis	Gross deformity of lower half of stomach with large ulcer crater	Very large G.U. on lesser curve infiltrating pancreas. Pancreas nodular	Biopsy: no evidence of malignancy. Suggests base of chronic peptic ulcer. Died 19/12/48	Histology

TABLE III.—(*Continued*)

Case No.	Age and Sex	Date of Admission	Clinical History	*X*-ray Findings	Operation	Morbid Anatomy and Histology	Diagnostic Criteria
16	56 M.	10/1/49	8 months before admission: pain under left costal margin every day, unrelated to meals	Large ulcerating filling defect near incisura	Carcinomatous ulcer straddling lesser curve in pre-pyloric region	Large pre-pyloric ulcer with raised edges and thick fibrotic base. Histology: ulcer-cancer	Histology
17	59 M.	25/2/49	1 year's history of pain 1½ hours after food and at night, sometimes relieved by alkaline powder. Recent change to constant pain	Large nodular mass in region of pyloric canal	Large pre-pyloric neoplasm invading pancreas and omentum	Large simple pre-pyloric ulcer with anaplastic adenocarcinomatous changes in the edges (ulcer-cancer)	Histology
18	49 M.	9/10/47	Pernicious anaemia, under treatment since 1932. 7 weeks' dyspepsia	Pyloric obstruction	Large pre-pyloric neoplasm, involving one side of a possibly benign ulcer	Adenocarcinoma, Broders I. Appearances consistent with its origin in a benign ulcer	Histology
19	44 M.	19/1/46	2½ years' vague indigestion. 1½ years' stabbing epigastric pain 2 hours after meals, relieved by alkalis. 7 months previously: haematemesis and melaena, relief of symptoms with rest in bed	Pre-pyloric ulcer—nature uncertain	Pre-pyloric ulcer	Naked eye: chronic gastric ulcer. Histology: ulcer-cancer	Histology
20	74 M.	25/11/38	Admitted with perforation. No previous history of indigestion		Closure of perforation in pre-pyloric region just proximal to a carcinomatous mass	Macroscopic: appearances suggest an ulcer. Histology: evidence of carcinoma arising at the site of a simple ulcer	Histology
21	68 F.	18/3/42	3 months before admission: epigastric pain after meals, worse at night. Frequent small vomits and steady loss of weight	Filling defect of pyloric antrum with gastric stasis	Pre-pyloric ulcer with thickened edges	Pre-pyloric ulcer with rolled edges. Anaplastic signet-celled carcinoma arising in the margins of a chronic ulcer	Histology
22	66 F.	14/5/40	1 year previously: flatulence and indigestion	Pre-pyloric obstruction due to a mass	Pyloric stenosis and ulcer on lesser curve causing hour-glass stomach	Hour-glass stricture upper part of body, with a proximal chronic ulcer. Adjacent to this is an adenocarcinoma. Macroscopic stricture of pylorus without pathological changes at microscopy	Histology
23	62 F.	25/3/47	30 years previously: perforated gastric ulcer. 7 months previously: pain left side unrelated to meals but relieved by alkalis. Later developed constitutional symptoms	Constant filling defect pyloric antrum	Stony-hard mobile mass just above pylorus	Chronic gastric ulcer with carcinoma infiltrating base. Lymph nodes involved	Histology
24	47 M.	7/3/42	20 years' dyspeptic history with remissions. 12 years previously: perforation; surgical closure. Continued to have dyspepsia. 10 weeks before admission: alteration in character of dyspepsia	Large G.U. adhesions to pancreas and gross deformity of pylorus (two examinations)	Biopsy of gland in neck	Anaplastic carcinoma	History
25	73 F.	21/9/46	Pain after meals for nearly all her life. 6 years previously: increasing severity of pain with many remissions. 4 months previously: frequent vomiting	Ulcer crater on middle third of lesser curve and pyloric stenosis	Polypoid pre-pyloric carcinoma. Ulcer on lesser curve	Adenocarcinoma pyloric region and simple gastric ulcer on lesser curve	History. Histology
26	73 F.	17/7/40	No details—patient admitted moribund			Old G.U. scar halfway along lesser curve. Pyloric carcinoma extending up to lower edge of scar	Histology

Discussion

It is clearly impossible to say that in any of the present group the carcinoma did not originate in a chronic peptic ulcer. However, so far as the site is concerned, the distribution is that of carcinoma. This suggests that a large number of the cases may have been carcinoma unrelated to preceding peptic ulcer. There are two pieces of evidence to support this possibility. The first is that half of the patients had clinical histories compatible with the diagnosis of carcinoma of the stomach arising *de novo*. Secondly, three of the patients had chronic peptic ulcers which were distinct from their carcinoma. A further small additional point is that one case had suffered from pernicious anaemia for many years, and it has been clearly demonstrated that chronic peptic ulcer does not occur in that disease.

The results of the fractional test meal show that this group of patients contained a large proportion (57%) with normal or high levels of acid. By some workers the finding of free acid has been thought to favour the diagnosis of "ulcer-cancer," but an alternative possibility exists—namely, that the presence of normal acidity greatly increases the chance of peptic ulceration of gastric carcinoma. It is true that some pathologists have claimed that they can distinguish such an event from the appearance of a true "ulcer-cancer," but Palmer and Humphreys (1944) claim that all diagnostic features of an "ulcer-cancer" can occur in ulcerating carcinoma.

It is reasonably certain that the data can be explained only in terms of one of the following possibilities: (*a*) that chronic peptic ulcers of the pre-pyloric region are extremely liable to become malignant; or (*b*) that

pre-pyloric carcinomata frequently undergo peptic ulceration and may then present with the histological features of so-called "ulcer-cancer."

We believe that the second possibility is inherently more likely. But, in any event, from a practical standpoint the main conclusion is unaffected by one's choice between these two possibilities. It is that pre-pyloric ulcers are commonly malignant and should be resected.

Summary

Among 375 patients with gastric carcinoma treated in the Radcliffe Infirmary there were 26 with some evidence that the neoplasm might have arisen in a simple ulcer.

There was good clinical evidence of chronic simple ulcer in only half the patients.

The site of the neoplasm for the group of 26 patients conformed with the distribution of carcinoma of the stomach and not with that of simple gastric ulcer.

In three cases the carcinoma had apparently arisen at a site different from that of a pre-existing simple ulcer.

We believe that most of these cases were examples of ulcerating carcinoma. In any event, the majority were pre-pyloric, and it is evident that pre-pyloric ulcers should be deemed malignant and treated by surgical resection.

We wish to thank the physicians and surgeons of the Radcliffe Infirmary for permission to make the study out of which the present article arises.

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THE USE OF ORAL CORTISONE IN PAEDIATRICS

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Since the preliminary report describing the effects of cortisone on 14 adult patients with rheumatoid arthritis was made by Hench, Kendall, Slocumb, and Polley in April, 1949, much work recording the action of the drug in this and numerous other diseases has been reported. However, the use of a microcrystalline suspension of cortisone acetate to be administered intramuscularly either once or twice daily presented an obvious disadvantage for prolonged therapy, especially in children, so that when limited supplies of cortisone became available in tablet form the opportunity arose to test its therapeutic efficiency by mouth.

Three children with rheumatoid arthritis, one child with acute rheumatic pericarditis, and one child with nephrosis were given 25-mg. tablets of cortisone acetate ("cortone"—Merck and Co.) once, twice, or three times daily as required. The tablets are slightly bitter if dissolved in the mouth, but were easily swallowed whole by the older children. They were given crushed in milk to the two younger children. No gastric intolerance was noted.

Case 1

A 12-year-old girl was admitted to hospital on January 27, 1951, because of swelling, deformity, and restricted movement of her wrists, elbows, fingers, knees, and ankles. She had been ill since July, 1949, when vague pains occurred in several of her joints. Swelling of the knees, associated with pyrexia, was first noted in January, 1950. A diagnosis of acute rheumatic fever was made and she was admitted to another hospital. Although her fever subsided with salicylate therapy, her knees remained swollen and her ankles also became similarly affected. During the summer months her general condition improved. She was allowed to go home, but was unable to walk about very much because of the swelling of knees and ankles. In October, 1950, her wrists and fingers also became swollen and were restricted in movement. She was readmitted to hospital, where a diagnosis of rheumatoid arthritis was made and gold therapy was begun. She was reported to be worse after the second injection, and so treatment was discontinued. She was transferred to the Royal Manchester Children's Hospital for cortisone therapy.

On admission (January 27, 1951) she was a poorly nourished, chronically ill-looking child with dryness and desquamation of the skin of the arms and legs and temperature of 99° F. (37.2° C.). The heart was normal. There was no lymphadenopathy or enlargement of the spleen. There were full movements of the neck and, so far as could be ascertained, full movements of the spine. The elbows and wrists were swollen and all movements were severely limited. The shoulder-joint movements were also restricted. All fingers showed fusiform swelling. The hips and knees were fixed in flexion; the latter were grossly swollen, were incapable of extension, and had no more than 2½ in. (6.3 cm.) separation. The ankles were also swollen, with marked foot-drop and hardly any dorsiflexion. There was slight pitting oedema of the dorsum of each foot.

Her blood pressure was 105/75 and the sedimentation rate 45 mm. in one hour. The haemoglobin was 54% (Haldane), with 4,490,000 red blood cells and 10,400 leucocytes per c.mm. The eosinophils were fewer than 5 per c.mm. Radiographs showed soft-tissue swelling around the joints, no narrowing or alteration of joint spaces, and severe rarefaction of all the long bones. Electrocardiograms were normal.

On February 10 cortisone was started. She was given 300 mg. by mouth in the form of four 25-mg. tablets three times a day. This was continued for four days. She was then given 150 mg. daily for three days and 100 mg. daily for seven days, so that she received 2.35 g. by mouth in 14 days.

Within 24 hours of the beginning of treatment her temperature became normal and remained between 97 and 98° F. (36.1 and 36.7° C.) throughout the course. Within 48 hours pain in the affected joints was much less. Whereas, before treatment, passive movements had made her wince with pain, the joints, although restricted in mobility, could now be moved without hurting her. On February 13, after 72 hours' treatment, all joints except the right ankle and left elbow measured less in circumference and the range of movement had definitely increased. She seemed much brighter mentally and began to take an intelligent interest in her progress and to co-operate with the physiotherapist. On February 16, after one week's treatment, she could separate her knees by 3½ in. (8.9 cm.) and the swelling of the joints was decreasing. There was an almost complete range of movement in the wrists, although some swelling was still present. The fingers had very slight fusiform swelling and the elbows seemed normal in shape and mobility. The skin was much improved in texture. For the first time she began to knit and could comb her hair, and she could sit on the side of her bed or in a chair. At the end of the two weeks' therapy her upper limbs seemed to be perfectly normal in all respects, apart from a weakness of the hand-grip due to wasting of the small muscles of the hand. Her

knees were beginning to straighten and could be separated by 10½ in. (26.7 cm.). The ankles showed full range of movement.

During treatment, apart from the slight increase in oedema of the dorsum of both feet towards the end of the second week and an increase in blood pressure from 105/75 to 115/75, there were no serious side-effects. There was some rounding of the face and an increase in appetite by the end of the first week. Her haemoglobin rose from 54% to 80% (Haldane), her red blood cells from 3,490,000 to 4,160,000 per c.mm., and her leucocytes from 10,400 to 21,600 per c.mm. in two weeks. Her E.S.R. dropped from 45 mm. to 6 mm. in one hour after one week's treatment and to 4 mm. in one hour after two weeks. The eosinophils, fewer than 5 per c.mm. before treatment, remained at this level until the last three days of the two weeks' course, when with a lower dose of cortisone they rose to 20 per c.mm. There was no change in the fasting blood sugar, and no glycosuria.

It was decided (February 24), after two weeks' treatment, to reduce the dose of cortisone to as low a level as possible consistent with the maintenance of improvement. Accordingly 50 mg. (two tablets) daily was given for seven days, and as no deterioration in condition was noted the dose was reduced to 25 mg. (one tablet) daily.

However, after four or five days it became apparent that she was not so well. Occasional pains in the wrists and shoulders occurred, and some swellings of the right elbow and right wrist were noted. Loss of mobility was detected in these joints and also in both knees. Spikes of fever were recorded, and the E.S.R. rose to 20 mm. in one hour. On March 12, therefore, the dose of cortisone was increased to 100 mg. (two tablets twice daily), and after four days' treatment it was considered that her condition was restored. From March 16 to April 7, 50 mg. (two tablets) daily was given, and this seemed to be the amount required to suppress all disease activity.

Treatment had to be discontinued on the latter date as no further supplies of cortisone were available, and again, four days later, she began to complain of pain in the joints, peaks of fever were recorded, and decreased mobility of the joints was noted. At the time of writing (May, 1951) the knees can be abducted only 2 in. (5 cm.) from each other, her fingers show the original fusiform condition, and her other joints are slowly returning to their pre-treatment condition.

Case 2

A 3¾-year-old girl was admitted to hospital on January 27, 1951, because of swelling and restricted movement of her wrists, fingers, hips, knees, and ankles. Apart from measles at the age of 7 months and tonsillitis in April, 1950, she had been a healthy child. In August, 1950, she became listless and fretful, complaining of pains in the hands, knees, and ankles, and screaming if her limbs were touched. A diagnosis of rheumatoid arthritis was made, and she was in bed for 14 weeks at home before being admitted to another hospital in November, 1950. She was transferred to the Royal Manchester Children's Hospital for cortisone therapy.

On admission (January 27) she was ill-nourished, fretful, and irritable, with marked wasting of the small muscles of the hands and legs, a retracted abdomen, and dry scaly skin. Her temperature was 98.8° F. (37.1° C.). The heart was normal, the spleen was not palpable, and no enlarged lymph nodes were present. Her wrists were swollen, the fingers were fusiform, and movements of these joints were restricted. The shoulders and elbows were normal. The left hip was fixed and internally rotated, while both knees were swollen and fixed in flexion. Both ankles were also swollen and had a limited range of movements. Any attempt to examine her or elicit passive movement was resisted. The E.S.R. was 48 mm. in one hour. The haemoglobin was 68% (Haldane), the red cells numbered 3,700,000 per c.mm., and the white cells 10,400 per c.mm., the eosinophils being fewer than 5 per c.mm. Radiographs of the affected joints showed no diminution or alteration in the joint spaces, but there were severe rarefaction of bones and some soft-tissue swelling. The head of the left femur seemed high in the acetabulum but was not subluxated. On February 12 cortisone was started. She was given 150 mg. by mouth in the form of two 25-mg. tablets three times a day. This was continued for four days, and then she was given 100 mg. daily by mouth for eight days, so that in 12 days she received 1.4 g. of cortisone. Her temperature remained normal throughout treatment. On February 14, after 48 hours, although she was still fretful and irritable, the wrists could be passively moved without evoking screams of pain.

Two days later the movements of the wrists and fingers were much improved, but fusiform swelling of the latter was still very obvious. The knees and ankles seemed unchanged, except that she would allow examination without screaming.

On February 19, although minimal fusiform swelling of the fingers was still present, all movements of the upper limbs seemed normal. The patient was beginning to eat and seemed much brighter and happier. The left hip, however, appeared to be internally rotated more than at first, and a repeat radiograph showed subluxation of the head of the femur. On orthopaedic advice the left hip was put on traction.

The E.S.R. dropped from 45 to 12 mm. in the hour in one week and rose to 14 mm. in two weeks. In this period her haemoglobin rose from 68% to 82% (Haldane), her red blood cells from 3,700,000 to 4,500,000 per c.mm., and her leucocytes from 10,400 to 26,000 per c.mm. The eosinophils varied between 5 and 20 per c.mm. during the period of treatment. There were no side-effects apart from rounding of the face ("moon facies").

On February 24 the dose was reduced to 50 mg. daily (one tablet twice a day), and on March 3 to 25 mg. (one tablet) daily. With this amount she remained symptom-free, bright, and happy, with maximal mobility of her joints and no side-effects. On April 7 supplies of cortisone were exhausted, and treatment with it had to be discontinued. Three days after cessation of the treatment the eosinophils, which during treatment had remained below 50 per c.mm., now rose to 130 per c.mm., and have remained above 50 per c.mm. ever since. The fingers have again become fusiform, the wrists have become swollen and limited in mobility, and while the patient was being nursed on a special abduction frame the knees and ankles have almost reverted to their pre-treatment condition.

Case 3

An 8-year-old girl was admitted to this hospital on March 9, 1951, with a three-year history of pains in the hands, feet, shoulders, and neck. After a sore throat in April, 1948, she began to complain of pains in all her joints in June, and was admitted to another hospital in this city. Her temperature varied between 100 and 105° F. (37.8 and 40.6° C.), the E.S.R. between 50 and 60 mm. in one hour, and there were swelling and tenderness of the wrists, knees, and ankles. A diagnosis of acute rheumatic fever was made. For three months she was treated with salicylates, sulphonamides, and penicillin without any change in her condition, but slowly during October and November there was a gradual improvement, with subsidence of fever, return of joints to normal, and ability to walk. She was allowed to go home, and remained well till the following summer, when she had a recurrence of joint pain and swelling associated with fever, necessitating her return to bed for a period of three months. She was readmitted to hospital, where a diagnosis of rheumatoid arthritis was made, based on the swelling and deformity of her ankles, knees, and wrists, and the fusiform appearance of the fingers. By July, 1950, she had improved sufficiently to enable her to walk and to warrant her return home, continuing physiotherapy as an out-patient.

On January 30, 1951, she was readmitted to hospital with an acute exacerbation of symptoms, tachycardia, and pyrexia, all of which tended to subside during the next month. She was transferred to the Royal Manchester Children's Hospital on March 9, 1951, for cortisone therapy.

On admission she was a pale undernourished child with palpable glands in the groin, axillae, and neck. The heart was not enlarged and sounds were normal. Blood pressure was 95/65, and the tip of the spleen could just be felt. Her temperature and pulse rate were raised on admission, but settled to normal levels during the subsequent week.

Neck movements, backwards and forwards and from side to side, were restricted. Wrists, elbows, knees, and ankles were swollen and severely limited in movement. All fingers showed typical fusiform swelling. Appetite was poor.

Blood investigations showed: haemoglobin, 60% (Haldane); 3,280,000 red blood cells per c.mm.; 18,400 white blood cells and 40 eosinophils per c.mm.; E.S.R. 84 mm. in one hour.

Cortisone therapy was started on March 17. Three 25-mg. tablets were given orally morning and night and two at midday, making 200 mg. a day, for three days. Within 48 hours the girl was brighter, and was talking to other children and the staff. Although there was no increase in range of movement, pain on passive movement of all joints had disappeared.

After three days' treatment the eosinophil count had dropped to 1 to 2 per c.mm. and some increase in range of movement of all the joints was noted. She was then given 150 mg. (two tablets thrice daily) orally for three days, and 100 mg. (two tablets twice daily) for 11 days. During this period there was a steady increase in range of mobility of all affected joints and a gradual diminution in swelling. On March 23, after a week's treatment, the E.S.R. dropped to 12 mm. in one hour, and on April 4, after 17 days' treatment, she began to take a few halting steps. On this day the dose of cortisone was reduced to 50 mg. daily (one tablet twice a day) in the hope that dosage could be maintained at this level, but four days later supplies of cortisone became exhausted and treatment had to be abandoned. She therefore received 2.4 g. of cortisone over a 22-day period.

The improvement in general behaviour and mentality was striking, being noted within 48 hours of the introduction of treatment. The temperature remained normal throughout and her blood pressure did not vary. Her weight increased from 32 lb. 2 oz. to 34 lb. 12 oz. (14.6 to 15.8 kg.) by the sixth day of treatment and to 35 lb. 12 oz. (16.2 kg.) by the end of treatment, but there was no oedema and the gain in weight was attributed to marked improvement in appetite. No side-effects were noted. The eosinophils remained low until the dose of cortisone was reduced to 100 mg. daily, when there was a slight rise in the eosinophil count and a further rise when the dose was dropped to 50 mg. daily, but there was no great increase and no evidence of the "rebound" phenomenon after cessation of treatment.

Four days after treatment was stopped it was noted that the child was not as bright or as happy as formerly, and she refused to make any attempt to walk because of pain in her knees and ankles, whereas formerly she had been eager to do so. A week after treatment was discontinued she began to show evening elevations of temperature, which have persisted ever since, and at the time of writing, one month later, joint movement is almost back to its pre-treatment range and swelling is almost as severe as formerly. The E.S.R. has risen to 93 mm. in one hour.

Case 4

An 11-year-old boy was admitted to hospital on February 11, 1951, having been listless and off colour since an attack of influenza in mid-December and tonsillitis in January, for which he had received penicillin therapy. One week before admission he had complained of pains in the shoulders and abdomen, but swelling of the joints had not occurred. He was reported to have had an attack of rheumatic fever in 1948 necessitating rest in bed for five weeks at home.

On admission his temperature was 99.5° F. (37.5° C.) and pulse rate 100. There were no nodules or erythematous rashes. The heart was not enlarged, but a systolic murmur (grade 3) was noted at the apex. Examination of the blood showed 82% haemoglobin (Haldane), 4,000,000 red blood cells, 12,600 white blood cells, and E.S.R. 102 mm. in one hour.

His condition remained unchanged until February 18, when in the evening he complained of pains in the left side of the chest. His temperature rose to 101° F. (38.3° C.) and his pulse rate to 120. A friction rub was audible all over the praecordium. During the next few days his temperature remained above 100° F. (37.8° C.) and his pulse rate above 120, and by February 24 his condition had deteriorated. He was orthopnoeic and slightly cyanosed. His heart was grossly enlarged, the borders of cardiac dullness to percussion extending into the axillae on both sides, beyond the maximal impulse that could be felt in the fifth left intercostal space 7 cm. from the mid-sternum. A systolic thrill and a to-and-fro friction rub were noted over the central precordial area, and a harsh systolic murmur was audible at the apex. Pulsus paradoxus was observed, and the blood pressure was 110/55. Both lung bases were dull to percussion, and an area of bronchial breathing and increased voice conduction could be made out at the left base. The neck veins were engorged to a point half-way between clavicle and jaw, while the liver edge was easily palpable. There was no oedema or ascites. The E.S.R. was 99 mm. in one hour, white cell count 21,200, and eosinophils 5 per c.mm. Blood culture was sterile. An *x*-ray film of the chest showed gross cardiac enlargement with evidence of pericardial effusion.

A low-salt diet was ordered and cortisone therapy was started. Three 25-mg. tablets were given morning and night and two tablets at midday, so that he received 200 mg. daily for two days.

On the second day of treatment the temperature reached only 99° F. (37.2° C.) and he seemed a little more comfortable. After two days' treatment there was a distinct improvement. The temperature was normal; tachycardia, however, was still present, but there was no dyspnoea or cyanosis. The maximal cardiac impulse was not as tumultuous or diffuse, and could be located 5 cm. to the left of the sternum in the fifth space. Pericardial friction had disappeared; a systolic murmur only was audible at the apex. Jugular venous pressure was normal. The liver was no longer palpable and no oedema had occurred.

X-ray films confirmed the diminution in cardiac size. It was felt that, as some improvement in cardiac function had occurred, the danger of a cortisone-induced salt retention precipitating cardiac failure was less likely, and the dose was increased to four tablets three times a day (300 mg. daily), which was given for four days.

On March 2, after six days' treatment, rounding of the face was noted. The E.S.R. was 45 mm. in one hour. Temperatures had been normal since the second day of treatment, but the pulse rate was still 110. The size of the heart appeared to be unchanged. Jugular venous pressure seemed to be slightly raised again and the liver edge was palpable. Moist sounds were noted throughout both lungs. Mersalyl, 0.5 ml., was given intramuscularly, and after a good diuresis on the two subsequent days signs of congestion disappeared. Cortisone was reduced to 150 mg. daily (two tablets three times a day) for four days and then to 50 mg. daily (one tablet twice a day) for four days. The patient therefore received a total of 2.4 g. in 14 days. The eosinophil count, which had remained low during the first 10 days' treatment, began to rise during the last four days, when low doses (50 mg. daily) were given.

On March 6, before the cortisone dose was reduced and despite continued clinical improvement, there was a

secondary rise in E.S.R., recorded as 58 mm. in one hour on that date and 106 mm. 10 days later.

During the week after cessation of treatment he had irregular peaks of temperature, a further rise in pulse rate, and an increased respiratory rate, and complained of occasional joint pains. These manifestations gradually subsided, and up to the time of writing he has been asymptomatic and afebrile. The pulse rate has dropped to 90 and the E.S.R. has fallen to 70 mm. in one hour. The maximal cardiac impulse is now 6 cm. from the mid-sternum just outside the mid-clavicular line, and systolic and diastolic murmurs have become recognizable at the apex.

Case 5

A 2½-year-old boy was admitted to hospital on February 14, 1950, with a four to five months' history of recurring bouts of puffiness of the face and legs. Apart from frequent colds, and sore throats for a short period 18 months previously, his general health and development had been satisfactory.

On admission he showed oedema of the eyelids, face, hands, and feet. There was some ascites. The heart and lungs were normal. Blood pressure was 125/85. The urine contained 3 g. of albumin and scanty red blood cells. His weight was 35 lb. (15.9 kg.). The blood contained 86% haemoglobin (Haldane) and 13,400 white cells per c.mm. Blood urea was 25 mg. per 100 ml., serum cholesterol 400 mg. per 100 ml., total serum protein 5.49 g.%, serum albumin 1.8 g.%, and serum globulin 3.69 g.%, the A/G ratio being 0.49.

During the next month his oedema fluctuated in severity, but on April 2, following an attack of bronchopneumonia with high fever seven days previously, a diuresis began and he lost 8 lb. (3.6 kg.) in weight. He was discharged from hospital on April 13, with slight oedema of his legs only, and 1 g. of albumin in his urine. His serum cholesterol was 680 mg. per 100 ml., and his total serum proteins were 3.71 g.%, with an A/G ratio of 0.3.

He remained well for one month at home and was then readmitted to hospital on May 16 with recurrence of oedema and ascites. The urine showed 5 g. of albumin and scanty red cells. Throughout May, June, and July he experienced numerous exacerbations and remissions but no true diuresis. His serum cholesterol reached 920 mg. per 100 ml. on September 23, and between that date and the end of the year he was transfused on several occasions with concentrated plasma without any effect. He had a moderate diuresis one week after an attack of mumps in January, 1951, but by mid-February his oedema and ascites were as marked as previously. His weight was 38 lb. 3 oz. (17.3 kg.). Blood pressure was 115/75.

On February 15 cortisone was started. Four 25-mg. tablets were given three times daily for three days, followed by two tablets twice daily for five days, and then one tablet was given morning and night on the last day of a nine-day course, so that he received 1,450 mg. in all.

His weight remained unchanged throughout treatment and his oedema and ascites did not vary. His blood pressure increased from 115/75 to 130/90. His eosinophils, 250 per c.mm. before treatment, dropped to fewer than 5 per c.mm. 24 hours later, remaining low throughout the period of treatment and increasing thereafter. Three days after cessation of treatment diuresis began and he lost over 7 lb. (3.2 kg.) in weight. The urinary albumin decreased to 1 g. and the blood pressure returned to 110/70. During the next six days he lost all his oedema, and when discharged from hospital on March 7 he weighed 28 lb. (12.7 kg.), showed a little ascites only, and had less than 1 g. of albumin in his urine.

When seen in the out-patient clinic on April 19 he was free of oedema and ascites. His urine contained 0.5 g. of albumin, and a blood examination showed a serum cholesterol of 170 mg. per 100 ml., and serum proteins of 5.72 g.%, with an A/G ratio of 1.5.

Discussion

Since Hench's original report two years ago, the striking benefit produced by injections of cortisone (17-hydroxy-11-dehydrocorticosterone; compound E) in various diseases has been fully confirmed. Thorn and his co-workers (Thorn *et al.*, 1950) have reviewed the clinical usefulness of the hormone. Suppression of the manifestations of rheumatoid arthritis has been confirmed both in America (Boland and Headley, 1949) and in this country (Copeman *et al.*, 1950). Juvenile rheumatoid arthritis has responded to this treatment in the same way as the adult form (Freyberg, 1950; Rosenberg, personal communication, 1950). The use of an oral form of cortisone, however, is much to be preferred in the treatment of children, and in the first three cases here reported the same striking beneficial results were demonstrated with the use of the hormone in tablet form. Moreover, improvement occurred as quickly after oral therapy as when parenteral therapy was used. After only 48 hours' treatment, passive movements of the affected joints could be carried out with less pain, indicating a reduction in stiffness of the muscles and joints and lessening of tenderness and pain on motion. After 72 hours' treatment there was increased mobility and some diminution in swelling.

The initial dose of cortisone was 300 mg. daily in Case 1, 200 mg. daily in Case 3, and 150 mg. daily in Case 2, and a substantial reduction in dose was made after the first three to four days. Cortisone administered by mouth was highly effective in suppressing disease activity without serious side-effects, and control could be maintained by giving 50 mg. daily to Case 1 and 25 mg. daily to Case 2, which meant in effect giving one or two tablets a day—a simple enough procedure to keep so serious a disease in abeyance. Relapse occurred, however, when therapy was reduced below this point and when it had to be discontinued entirely. The sedimentation rate, haemoglobin, red cells, and white cells reacted in the same way with this type of therapy as has been reported with the use of intramuscular injections of cortisone (Hills *et al.*, 1948: Thorn, 1949). In all three children the E.S.R. became normal after one week's treatment, but began to rise again after treatment was discontinued. There were substantial increases in haemoglobin and red blood cells in all three patients.

The child (Case 4) with acute pericarditis showed a dramatic initial response 48 hours after treatment with 200 mg. daily of cortisone was begun. Pericardial friction disappeared, temperature returned to normal, dyspnoea and cyanosis were relieved, and there was some diminution in cardiac size. His condition appeared to be stationary during the remainder of the 14-day period of treatment. During the week after treatment, however, there were signs of increased activity as shown by occasional pains in the joints, spikes of fever, and an increasing pulse rate. During the two months that have elapsed since then there has been a slow and gradual decrease in cardiac size, although systolic and diastolic murmurs persist. The pulse rate has returned to normal, the temperature has remained within normal limits, and the course of the disease has undoubtedly been shortened.

The E.S.R. showed a characteristic response. After a preliminary fall from 99 to 49 mm. in the hour there was, despite continued clinical improvement, a secondary

rise to 106 mm. 14 days later. Since then there has been a slow and steady decrease to normal levels. The result achieved in this case, using 200 mg. of cortisone daily for the first two days—a dose similar to that described by Hench using parenteral therapy—was comparable to that described by Barnes (1950), and by Massell *et al.* (1950), using intramuscular injections. By virtue of its salt- and water-retaining properties, and in the presence of impaired cardiac function, cortisone is capable of producing congestive failure, but, by the use of a low-salt diet and a mercurial diuretic at the first sign of congestion, serious side-effects were prevented.

The child (Case 5) with nephrosis gave a 16-months history of exacerbations and remissions of his oedema and ascites, showing characteristic diuresis after episodes of high fever associated with pneumonia and mumps. On no occasion, however, had diuresis been complete nor had albuminuria entirely disappeared. Chemical examination of the blood showed abnormalities. Three days after a nine-day period of administration of oral cortisone a diuresis began during the course of which he lost all his oedema and ascites. Albuminuria virtually disappeared and blood tests returned to normal. At the time of writing he had remained well for nearly three months, the longest remission he has ever experienced.

A similar diuretic response has been obtained in this disease by Keith *et al.* (1950) and Barnett and his co-workers (1950) using parenteral cortisone, but the advantage of being able to give the hormone by mouth instead of by injection to an oedematous child need hardly be stressed.

Cortisone given by mouth, therefore, was capable of producing the same type of response as when given by injection in patients suffering from rheumatoid arthritis, rheumatic fever, and nephrosis. Absorption from the gastro-intestinal tract appeared to be certain and reliable provided the total daily dose was divided and given in two or three portions. Its actions came into effect as quickly as when parenteral administration was used. No gastric intolerance was noted and side-effects were minimal, but these were no different from those noted with the other type of cortisone administration, and were perhaps less marked. Slight elevation of the blood pressure was noted in one patient with rheumatoid arthritis and in the patient with nephrosis during the period of treatment, but there was an immediate return to normal after treatment had ceased. The danger of producing salt- and water-retention and precipitating cardiac failure in patients with impaired cardiac function is always present, but this danger is probably more easily avoided when the dose of cortisone can be administered in divided amounts by mouth. Rounding of the face, increase in appetite, and a brightening of mental outlook were noted in all patients during the first week's treatment—an effect similar to that noted when the drug was given by injection.

Freyberg *et al.* (1950) used 100-mg. tablets in the treatment of four adult patients with rheumatoid arthritis, and considered that in all respects the clinical effects of orally administered cortisone were comparable to those of the hormone given parenterally. Kuzell and Schaffarzick (1950) treated 11 patients with various types of arthritis with the 25-mg. tablets and claimed to obtain the best results by giving two-thirds of the daily dose on rising and one-third on retiring. They felt that 1.25 to 3 mg. of cortisone given orally was required to equal the effect of 1 mg. given by injection. Boland and Headley, in a study designed to compare the effectiveness of the oral and intramuscular routes of administration of the drug, were able to suppress disease activity and maintain control in 22 out of 23 adults with rheumatoid arthritis, using the oral method, but they found that larger maintenance doses were needed when the drug was given by mouth.

Summary

Cortisone given in tablet form by mouth was capable of suppressing disease activity in three children with rheumatoid arthritis and one child with rheumatic pericarditis.

Control of the former disease was obtained by the administration of one to two tablets a day.

Diuresis was produced and remission obtained in one patient with nephrosis after a course of treatment with cortisone.

Oral cortisone was as quickly and as completely effective in the treatment of these diseases as parenteral cortisone, the same amount of the drug being found to be necessary, so long as the total daily dose was given in divided amounts two or three times a day.

The ease of administering a tablet preparation of cortisone, particularly for prolonged therapy in children, is stressed.

My thanks are due to Dr. Augustus Gibson, medical director, Merck and Co., New Jersey, U.S.A., who kindly supplied the tablets of cortisone acetate; to the physicians who referred the above patients; and to Professor Wilfrid Gaisford for permission to treat them and for valuable advice in the preparation of this report.

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In his annual report for 1950 the medical officer of health of Birmingham discusses social conditions in that city. Slum clearance is a pressing problem, for there are still 28,917 back-to-back houses. "Houses forming a continuous row abutting on to the street are separated at the rear by a 4½-in. wall from similar houses, and facing these across the courtyards are other little houses of similar type, all massed together and using w.c.s and washhouses in common." A survey carried out in 1946 showed that in the central ward of the city there were 36,000 houses, 18,265 of them being of the back-to-back type, 4,337 being without internal water, and 21,225 being without a separate w.c. The school medical officer of Liverpool, in his annual report for 1950, states that 24,849 children were found during the year to show some evidence of verminous infestation or were very dirty. Of the children examined by school nurses during cleanliness surveys 20.9% were found at least once during the year to be infested.

IRON METABOLISM IN PREGNANCY

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Haematological findings in the pregnant woman are difficult to assess. In the non-gravid state the normal range of variation in cell count and haemoglobin level is already generous. In pregnancy this range has to be increased and the scatter of values about the mean becomes widely dispersed Not only may individuals vary widely from the arbitrary normal, but considerable changes may take place in the same individual in a short time. In part the difficulty arises from the increase in plasma volume during pregnancy, which Dieckmann and Wegner demonstrated in 1934. This means that cellular and haemoglobin concentration per unit volume will change without altering the essential feature which we wish to assess—the total oxygen-carrying capacity of the blood. For this reason it would seem desirable to calculate the total circulating cell mass and total haemoglobin in assessing a pregnancy anaemia. Modern methods of determining blood volume, such as the Evans blue technique used by Thomson *et al.* (1938) or the agglutination method of Mollison *et al.* (1943), are reasonably accurate, but are laborious and require so much skill and care as to put them beyond consideration as routine procedures.

The blood picture in pregnancy is further confused by other established physiological changes. The leucocytes are increased (Gibson, 1937), the red-cell fragility is increased (Elliott, 1944), and so is the erythrocyte sedimentation velocity (Whitby and Britton, 1950). The plasma proteins fall (Ward and MacArthur, 1947), and so does the prothrombin level (Javert and Macri, 1941).

Also during pregnancy there are several new factors which tend to produce anaemias of various types. Foetal demands for iron strain the mother's capacity to metabolize this metal. Pregnancy is sometimes associated with a deficiency of hydrochloric acid in the gastric juice (Strauss and Castle, 1932, 1933), which leads to defective iron absorption. The capricious appetite of a pregnant woman may produce dietary idiosyncrasies whereby the intake of iron-containing foodstuffs is inadequate. Bethell *et al.* (1939) have shown the necessity of adequate dietary protein for normal haemopoiesis. Protein lack is common in many parts of the world, and the increased protein need of pregnancy is often the precipitating factor of an anaemia. Pregnant women are particularly exposed to the risk of haemorrhage, and are prone to such anaemia-producing conditions as the vomiting of pregnancy and toxaemia.

Clearly it is most difficult to assess the haematological state of a woman just when she is peculiarly liable to defects of haemopoiesis. In this context it seemed worth while to consider the blood picture of the pregnant woman in terms of her iron metabolism rather than of cellular production. Naturally this views only one facet of haemopoiesis, but it would be of interest if a description of this could be given. With this end in view we considered some of the literature on iron metabolism. The discovery of serum iron by Abderhalden (1898) was the starting-point for much valuable research into iron metabolism. As techniques were refined, workers in Europe and America were able to map out the physiological and pathological variations of this iron fraction. During the last decade the iron carrier has been identified as a specific subfraction of the β_1 globulins of the serum proteins. The use of radioactive iron isotopes as tracers by Hahn *et al.* (1940) and Granick's (1946) explanation of the mechanism of iron transfer to the blood stream from the intestinal lumen have further advanced our knowledge. We are approaching an understanding of the interrelationship of the metabolism of iron and copper.

Investigations into the iron metabolism of pregnancy have, however, been patchy and the results contradictory. During 1950 an investigation was undertaken to determine the normal levels, at various stages of pregnancy, of serum iron, the iron-binding capacity of the serum, the serum copper, and the free erythrocyte protoporphyrin in patients attending the antenatal service of Hammersmith Hospital (Ventura and Klopper, 1951a). In the course of these investigations some anaemias of pregnancy were discovered. Similar determinations in these cases showed a picture differing from the normal. The purpose of the present communication is to present a study of these cases and to trace the regeneration of the picture when intravenous iron is given.

Material

The patients attending the antenatal department of this hospital were haematologically assessed by Professor G. A. Elliott in 1944, and by Professors Young, King, *et al.* in 1946. As the type of population has remained the same, we assumed that we were dealing with a group whose characteristics were known. In deciding whether any particular case was anaemic or not, we compared the findings to the standards set up for this population by these workers, as well as with the general standards proposed by Whitby and Britton.

All pregnant women attending the department have a routine haemoglobin estimation done at their first visit—generally when between 10 and 16 weeks pregnant. A repeat estimation is performed at 36 weeks. Any case having a haemoglobin of less than 10 g. of haemoglobin per 100 ml. (68% Haden) was brought under review. A red-cell and white-cell count was done, the packed cell volume and erythrocyte sedimentation rate were determined, and a stained film was examined. The usual indices were calculated—mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration. Any women found to have signs suggestive of anaemia during the course of routine antenatal care were similarly investigated. We were able in this manner to identify 43 cases of iron-deficiency anaemia among the 1,804 cases delivered by the obstetric service of the hospital.

Techniques

Haemoglobin estimations were done by the alkaline-haematin method of Wu (1922) as recommended by Clegg and King (1942). The colour intensity was read

with a photoelectric photometer against a standard of artificial haematin. Serum iron was determined by using potassium thiocyanate. We found this reagent to be more sensitive than alpha-alpha-dipyridyl and orthophenanthroline, which are sometimes used. Our method for determining serum iron is discussed in detail elsewhere (Ventura and Klopper, 1951a).

Serum-copper determinations were made according to the method described by Cartwright *et al.* (1945); modified by using a simple 6/N hydrochloric acid extraction to free the copper from the serum proteins instead of the longer method using trichloroacetic acid.

The unsaturated iron-binding capacity of the serum is measured by determining the amount of iron which the serum proteins are capable of binding. Our method has been detailed elsewhere (Ventura, 1951).

The free erythrocyte protoporphyrin was determined according to the method of Grinstein and Wintrobe (1948).

Results

In 54 cases a haemoglobin level below 10 g.% was found. Some of these were very close to the critical level and on repeat examination were just above it. Such cases were put on oral iron therapy and kept under observation. If no further deterioration occurred we regarded them as low normals; eight cases were discarded in this manner.

Among the remaining 46 cases no examples of pernicious anaemia or other macrocytic anaemias were found. Reid and Mackintosh (1937) did not find any cases of pernicious anaemia in 1,108 pregnancies, and it is now generally accepted that in this country macrocytic anaemias rarely occur in pregnant women. Three cases were found to have haemolytic anaemias. One of these was a case of congenital haemolytic anaemia of obscure origin which had been under observation in the haematology department for many years and in which the pregnancy was incidental. The other two were mild cases of familial acholuric jaundice.

The remaining 43 cases were anaemias caused by disorders of iron metabolism. We found that these cases fell into two categories. The majority were classical cases of microcytic hypochromic anaemia. As we show later, biochemical analysis displayed a marked iron deficiency. This was readily corrected by the intravenous administration of iron. A smaller group (five cases) showed an aberrant pattern. Their red-cell counts fell *pari passu* with the reduction in haemoglobin, so that the colour index remained near unity; stained films presented a normochromic appearance and the cell size was not reduced. Further evidence of abnormal haemopoiesis was shown by an increased anisocytosis.

Normocytic Anaemia

The haematological findings of these five cases of normocytic anaemia are detailed in Table I. Bone-marrow smears prepared from two of the cases showed a normoblastic reaction. None of these patients complained of any symptoms suggesting anaemia, nor did they present any signs of the disease when examined. In all cases the pregnancy was well advanced, between 30 and 40 weeks. Previous investigations (Ventura and Klopper, 1951a) have shown that in patients attending this department the normal level of serum iron is 72 μg. at this stage of pregnancy. The mean of these five cases is 71 μg. and all are well within the range of normal variation.

TABLE I.—*Normochromic Anaemias*

Case	Age	Parity	Maturity	Hb	R.B.C.	C.I.	M.C.V.	S.I.	I.B.C.	Cu	Porp.
A	35	6	40 wks.	9·8	3·4	1·0	88·5	81	343	173	21
B	27	1	38 ,,	9·6	4·0	0·85	78·2	71	315	245	25
C	40	0	33 ,,	9·5	3·7	0·90	80·2	68	235	142	32
D	33	3	34 ,,	9·8	3·6	0·96	84·1	69	395	197	38
E	30	0	36 ,,	9·5	3·4	0·98	86·3	65	290	165	71

Hb = Haemoglobin in grammes per 100 ml. R.B.C. = Red blood corpuscles in millions per c.mm. C.I. = Colour index. M.C.V. = Mean corpuscular volume in cubic microns. S.I. = Serum iron in μg. per 100 ml. I.B.C. = Iron-binding capacity in μg. per 100 ml. Cu = Serum copper in μg. per 100 ml. Porp. = Free erythrocyte protoporphyrin in μg. per 100 ml.

In like fashion the other constituents show normal levels when compared with the established values.

The values for normal pregnancy at 30–40 weeks we found to be: unsaturated iron-binding capacity, 382 μg: serum copper, 255 μg.; protoporphyrin, 48 μg. It is presumed that these figures indicate that adequate transport iron is available for haemopoiesis and that the block in haemoglobin synthesis exists in iron utilization rather than in its absorption. Very little benefit can be expected from iron administration either orally or intravenously.

The diagnosis of anaemia is difficult to establish in these cases. It is not clear how much allowance should be made for the hydraemia of pregnancy in the individual case. Various authorities have put forward different minimal normal haemoglobin values for pregnancy (Dieckmann and Wegner, 1934; Adair *et al.*, 1936; Boycott, 1936; Bethell, 1936; Labate, 1940). Boycott in his paper stressed the importance of increased anisocytosis in the diagnosis of anaemia during pregnancy. This point was again emphasized by Elliott in working on material from this clinic. All five of the cases under discussion showed this characteristic. It may be, of course, that these borderline cases should be regarded as falling within the range of normal variation. We are concerned largely with the fact that the biochemical analyses show that these are not cases of deficient iron absorption, and that they are therefore not suitable for iron therapy.

Hypochromic Anaemia

The comparable findings in nine cases of hypochromic anaemia are summarized in Table II. Here the picture is quite different. The serum iron falls to a very low level. The iron-binding capacity of the serum proteins is considerably increased, and the level of serum copper rises above normal limits. As there is insufficient iron to combine with all the available protoporphyrin, the amount of free erythrocyte protoporphyrin is considerably raised. The picture of manifest iron deficiency

TABLE II.—*Hypochromic Anaemias*

Case No.	Age	Parity	Maturity	Hb	R.B.C.	C.I.	M.C.V.	S.I.	I.B.C.	Cu	Porp.
1	20	0	26 wks.	10	4·2	0·83	76	47	545	181	112
2	25	1	30 ,,	8	4·2	0·67	66	29	464	202	171
3	35	2	34 ,,	8·6	4·0	0·75	75	21	470	170	162
4	32	1	24 ,,	9·0	4·0	0·69	67	37	437	307	106
5	27	0	28 ,,	7·4	3·6	0·72	70	26	512	308	191
6	41	3	28 ,,	5·7	3·4	0·59	59	27	540	352	77
7	29	2	26 ,,	9·4	3·8	0·87	71	40	470	351	86
8	43	3	30 ,,	9·8	4·1	0·84	70	28	538	291	42
9	33	6	28 ,,	8·3	4·8	0·61		37			95

See notes to Table I.

is corroborated by the haematological findings. The aetiology of these anaemias is often obscure. Our cases suggested several possibilities. Cases 1 and 4 were achlorhydric, Case 8 had a history of heavy blood loss with previous confinements, and Case 9 was a multigravida. Cases 2, 4, and 6 were poor women living in overcrowded homes on a monotonous impoverished diet.

Whatever the cause of the iron impoverishment may be in the individual case, all responded in a satisfactory manner to the intravenous administration of iron. By this means all the faults in the mechanisms of iron metabolism below the level of utilization are short-circuited. As can be seen in Table III, the anaemia is

TABLE III.—*Response to Intravenous Iron*

Case No.	Stage in Treatment	Hb	S.I.	I.B.C.	Cu	Porp.
1	Before commencement	10 g.	47	545	181	112
	After 100 mg. iron	10·2	50	561	200	127
	After 500 „ „	12 g.	74	460	210	96
2	Before commencement	8·0	29	464	202	171
	After 100 mg. iron	8·5	35	471	200	169
	After 700 „ „	10·2	63	420	210	—
	„ 1,000 „ „	12·0	68	390	240	142
3	Before commencement	8·6	21	470	170	162
	After 200 mg. iron	9·1	25	470	166	184
	„ 300 „ „	10·2	42	410	150	102
	„ 500 „ „	11·2	41	432	142	131
4	Before commencement	9·0	37	437	307	106
	After 400 mg. iron	11·6	35	440	299	150
	„ 600 „ „	11·8	49	400	270	161
5	Before commencement	7·4	26	512	308	191
	After 100 mg. iron	8·0	30	475	320	251
	„ 300 „ „	8·9	45	412	278	240
	„ 700 „ „	10·5	58	420	260	180
6	Before commencement	5·7	27	540	325	77
	After 800 mg. iron	7·5	48	535	300	120
	„ 1,300 „ „	9·5	61	440	205	104
	„ 1,500 „ „	9·7	74	400	185	105
	„ 1,700 „ „	14·5	82	395	155	105
7	Before commencement	9·4	40	470	351	86
	After 100 mg. iron		32	500	280	63
	„ 400 „ „	10·5	48	475	250	107
8	Before commencement	9·8	28	538	291	42
	After 100 mg. iron	10·4	51	450	295	99
	„ 500 „ „	11·6	59	448	280	75
	„ 900 „ „	13·5	72	336	171	101

See notes to Table I.

corrected irrespective of whether it be due to depleted iron reserves, dietary shortcoming, or a breakdown in iron absorption. This table shows the state of iron balance in eight cases at various stages of their recovery when treated with weekly injections of 100 mg. of "ferrivenin." Case 9 is not shown, as her veins were unsuitable and the treatment had to be abandoned after two injections. All the other cases received between 500 and 2,000 mg., treatment being continued until their haemoglobin rose above 10.2 g.% at a minimum. Reticulocyte counts done after the second injection revealed a response of 3%–9%. Clinically the patients showed improvement; pallor improved, and such symptoms as breathlessness and giddiness were relieved. Serum-iron levels rose slowly to normal, while the iron-binding capacity of the serum and the serum copper fell from their abnormally high concentration. In the case of protoporphyrin the response was slow and uncertain. In general the trend was often downward, toward levels pertaining in normal pregnancy, but the pattern was not consistent.

The effect of ferrivenin on the regeneration of haemoglobin in the hypochromic anaemia of pregnancy was studied in a further 27 cases. The results are summarized in Table IV. The adult male is haematologically stable.

TABLE IV.—*Effect of Intravenous Iron on Haemoglobin Level*

Case No.	Initial Haemoglobin (g.)	Total Iron Given (mg.)	Final Haemoglobin (g.)	Rise per 100 mg. Iron (g.)
10	6·5	1,000	12·1	0·560
11	9·2	600	11·7	0·417
12	8·7	900	11·0	0·256
13	9·0	1,300	12·0	0·231
14	8·7	300	10·5	0·600
15	9·6	300	10·9	0·433
16	8·7	700	12·8	0·586
17	9·5	200	10·4	0·450
18	9·3	300	11·2	0·633
19	9·6	1,000	12·2	0·260
20	9·0	300	10·5	0·500
21	9·9	500	11·1	0·240
22	7·3	700	11·0	0·529
23	8·6	600	12·1	0·583
24	9·6	500	11·6	0·400
25	9·6	500	12·5	0·580
26	7·3	1,100	10·7	0·309
27	8·9	900	11·0	0·233
28	9·3	700	11·5	0·314
29	8·7	400	10·6	0·475
30	9·0	300	10·7	0·567
31	9·4	500	11·5	0·420
32	6·6	800	11·0	0·550
33	9·3	600	11·3	0·333
34	8·4	800	10·7	0·288
35	8·6	500	11·5	0·580
36	9·9	200	10·4	0·250

If given intravenous iron for an iron-deficiency state the injected iron will be quantitatively utilized. The expected rise in haemoglobin can be predicted with reasonable accuracy (Goetsch *et al.*, 1946). Simple haemoglobin estimations are an eminently satisfactory check on progress. If they do not correspond to predicted values some error in diagnosis or laboratory procedure has to be sought for. It is possible in these cases to calculate iron requirements accurately and so avoid overdosage with the possible danger of haemosiderosis. In the pregnant woman this state of affairs does not apply. The demands of the foetus for iron, and the hydraemia of pregnancy, introduce two new variables which make accurate forecasting of haemoglobin levels impossible.

Heath *et al.* (1932) have shown that in the non-pregnant state 24.5 mg. of iron is needed to raise the haemoglobin by 1% Haldane (0.16 g.) per day. On this basis a 100-mg. ampoule of ferrivenin should raise the haemoglobin by 4% (0.64 g.). Govan and Scott (1949) found that in pregnant women the highest response they obtained was 2.6% Haldane (0.416 g.), and they calculated that it would require nearly 40 mg. of ferrivenin to raise the haemoglobin by 1%. Our haemoglobin percentages were calculated on the Haden scale of 100% = 14.8 g., but, translating our values into Haldane equivalents, it can be calculated from the 35 cases in Tables III and IV that our average rise of haemoglobin per 100 mg. of iron was 2.7% (0.436 g.). By this calculation it would require 37 mg. of elemental iron to raise the haemoglobin of our cases by 1% Haldane.

We have published elsewhere a study of the urinary excretion of ferrivenin (Ventura and Klopper, 1951b). We found that only 3.5% of the iron injected is lost. Evidently the discrepancy between anticipated rise in haemoglobin and the rise actually found is due to iron loss to the foetus. On the basis of our calculations 12.5 mg. of each 37 mg. of iron injected went to the foetus. Naturally this figure applies only in the last quarter of pregnancy, when foetal demands are high.

Summary

In late pregnancy iron-deficiency states are difficult to assess by ordinary haematological investigations. The levels

of serum iron, the iron-binding capacity of the serum proteins, the serum copper, and the protoporphyrin were investigated in normochromic anaemia and in hypochromic anaemia. In true iron-deficiency states these show a characteristic pattern which is quite different from the normal. This characteristic pattern was outlined in nine cases of microcytic hypochromic anaemia, and the regeneration towards normal was studied when these cases were given intravenous iron.

We are indebted to Professor James Young and Professor E. J. King for access to their patients and for the facilities to do this work. One of us (S V.) is receiving a British Council grant. Mr. T. Simmonds kindly carried out all the haemoglobin determinations and cell counts.

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A note in the *New York Times Supplement*, November 4, describes some American experience with the new way of killing rats and mice with "warfarin." This contains dicoumarol, the blood anticoagulant often used in the treatment of thromboses, which was introduced for pest control by J. A. O'Connor in Malta in 1947. The anticoagulant is presented in the form of a food bait which is eaten fairly readily by animals over a period of time: internal bleeding occurs in 5 to 14 days, and they die from anaemia and shock, particularly if their normal blood volume is small, as is the case in rats and mice. The risk to pets is slight—a cat would have to eat several poisoned mice daily for at least a week to suffer ill-effects, while on farms the greatest danger is to hogs. There are estimated to be at least 300 million rats in the U.S.A., and one extremely successful rat-killing campaign in Texas is mentioned where 15 lb. of warfarin destroyed 550 rats. It is suggested that research should be carried out on other anticoagulants, which may prove more effective than dicoumarol in waging biological warfare on rodents.

DIABETIC GANGRENE

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There is still a tendency in many places to proceed at once to radical surgery in diabetic gangrene, mainly because it is felt that, as in senile gangrene, nothing less than amputation, usually of the above-knee type, will arrest the progress of the disease. It is our aim in this paper to show that conservative surgery has a very definite place in treatment, and that it will in most cases leave a useful limb with a minimum of disability.

Diabetic gangrene can be divided into two types: (1) those cases in which infection is the primary factor; and (2) those in which occlusive vascular disease is the exciting cause.

The former type is found among the younger patients and is much less common than senile diabetic gangrene. The arterial tree appears perfectly normal, and so are the pulsations throughout the limb. The gangrene is due to primary infection followed by secondary thrombosis of the digital vessels. Occasionally the condition is well advanced before the patient is seen, owing to the associated diabetic neuritis and its resultant hyposensitivity and loss of pain.

The treatment of these cases, no matter how advanced the gangrene may appear, is definitely conservative. If possible the sensitivity of the organisms should be determined in order to indicate the correct antibiotic and chemotherapeutic agents to be used, and *x*-ray examination is necessary to exclude the presence of suppurative arthritis or osteomyelitis of the phalanges and metatarsals. Surgical treatment is limited to complete excision of all gangrenous tissue and adequate drainage of the affected tissue planes.

These simple measures are usually effective and only in exceptional circumstances is amputation necessary. The diabetic condition demands very careful supervision owing to the profound disturbance of metabolic balance resulting from the infection, but we have found that stabilization takes place almost immediately the infection is controlled.

The latter type is that which occurs in elderly patients; in these, degenerative changes in the peripheral blood vessels lead to decreased vitality in the tissues and diminished resistance to apparently trivial infections. The diabetic condition is usually mild or moderate in degree and the insulin requirement often minimal; control by diet alone may be sufficient. It is in such cases that conservative treatment plays its most important part, especially where impaired myocardial and renal functions are present and may lead to post-operative complications. It has been our experience that limited surgery, aided by chemotherapy and antibiotics, will avoid the necessity for amputation in a large number of these patients. This experience is contrary to the not

uncommon view that amputation, and particularly above-knee amputation, is the only effective surgical treatment.

In most cases infection is not the dominating factor, and widespread infiltration is unusual. The gangrene is slowly progressive and generally remains limited to the area of the foot in which it began.

Treatment

Our routine treatment is as follows: (1) Penicillin or streptomycin is administered systemically, depending upon the organism sensitivity. (2) The state of control of the diabetes is reviewed. Effective and early control is much more easily obtained in these cases than in the primary infective gangrene in the young diabetic. (3) The foot is *x*-rayed. The presence or absence of bone necrosis is a guide to the extent of surgical treatment.

If there is no necrosis, purely nibbling surgery is performed and the necrotic tissue is thoroughly excised. The part is carefully inspected for deep sepsis, and infected tracks are laid open. Bleeding from the margins and base of the raw area is regarded as a good prognostic omen. The wound is cleansed with hydrogen peroxide, followed by the application of methylated ether. The final dressing is of tulle gras, with or without local penicillin.

If there is radiological evidence of bony changes in the phalanges and metatarsals, then the affected toe or toes with their respective metatarsals are amputated. If possible it is best to amputate through the proximal phalanx rather than disarticulate at the metatarso-phalangeal joint, as we have found that disarticulation has a tendency to impair the blood supply to the adjacent toe, and also that the exposed articular cartilage covering the metatarsal head necroses and delays healing.

Dr. Wilfred Oakley (personal communication) is of the opinion that when amputation of a toe is required there is much to be gained by removing all the other toes of the affected foot at the same time; this avoids troublesome recurrence at a later date. Joslin *et al.* (1946) recommend trans-metatarsal amputation in such cases for the same reason.

From our experience of 50 cases of diabetic gangrene we are profoundly impressed with the excellent results obtained by conservative surgery, especially in those patients with occlusive vascular disease who would normally be described as of the senile arteriosclerotic type. We have found that, provided the devitalized and infected tissues are removed completely and there is free haemorrhage from the edges and base of the area after excision, a satisfactory result with preservation of the limb may be confidently expected.

The accompanying Table shows details of 50 cases which have been treated as described above. A brief record of the first four is given to illustrate the methods which we adopt.

Case 1

A woman aged 70. Diabetic for 13 years, taking soluble insulin, 10 units twice daily. Admitted July, 1949, with a subcuticular abscess on the sole of the right foot, the result of a neglected callus. Blood pressure 210/100. Urine contained albumin ++. Blood urea, 50 mg. per 100 ml.

Procedure.—Incision of the abscess and evacuation of pus: cleansed with hydrogen peroxide and methylated

Details of 50 Cases

Case No.	Age	Sex	Site	Precipitating Factors	Treatment	Follow-up	Result
1	70	F.	R. 3rd toe	Infection and vascular	Amputation	1 year	Satisfactory (ambulant)
2	61	F.	R. great toe	Infection	Local	2½ years	Satisfactory
3	70	F.	L. 2nd toe, R. great toe	Vascular	Amputation	1½ ,,	,,
4	47	F.	R. 4th toe	,,	,,	1 year	,,
5	65	F.	R great toe	Infection	Local excision	2 years	Died (coronary occlusion)
6	55	F.	Dorsum R. foot	Infection and vascular	Excision and amputation	1½ ,,	Died (congestive heart failure)
7	63	M.	R. heel	Infection	Local	3 ,,	Died (coronary occlusion)
8	58	M.	L. great toe	Infection and vascular	Amputation	3 months	Satisfactory (ambulant)
9	72	F.	L. 2nd and 3rd toes	,, ,,	Local	2½ years	Satisfactory
10	51	F.	L. 2nd toe	Infection	,,	1 year	Satisfactory (ambulant)
11	57	M.	R. great toe	,,	,,	4 months	,, ,,
12	66	F.	L. 2nd, 3rd, and 4th toes	Vascular	Amputation	1 year	Died (coronary occlusion)
13	62	M.	R great toe	,,	,,	3 years	Satisfactory (ambulant)
14	16	M.	Dorsum R. foot	Infection (fulminant)	Local	6 ,,	,, ,,
15	53	F.	R. 3rd, 4th, and 5th toes	Infection and vascular	Amputation	2 ,,	,, ,,
16	66	M.	L. 1st interosseous	Infection (fungus)	Local	3 ,,	,, ,,
17	57	F.	R. 5th toe	Infection	,,	4 ,,	,, ,,
18	52	M.	L. 2nd and 3rd toes	,,	Amputation	3 ,,	,, ,,
19	75	F.	L. 5th toe	Vascular	,,	10 months	Died (congestive heart failure)
20	49	F.	R. 1st interosseous	Infection (fungus)	Local	5 years	Satisfactory (ambulant)
21	60	M.	R. great toe	Infection	,,	3½ ,,	,, ,,
22	80	F.	L. 2nd toe	,,	Amputation	2 months	Died (senility)
23	63	F.	R 1st, 2nd, and 3rd toes	Vascular	,,	1½ years	Satisfactory (ambulant)
24	69	F.	L heel	Infection	Local	2½ ,,	,, ,,
25	73	F.	R. 3rd toe	Vascular	Amputation	6 months	,, ,,
26	55	F.	R. 2nd toe	Infection	,,	2½ years	,, ,,
27	44	M.	R. 4th and 5th toes	,,	,,	3 ,,	,, ,,
28	67	F.	L. great toe	,,	Local	1½ ,,	,, ,,
29	71	F.	R. 2nd toe	Vascular	,,	5 months	,, ,,
30	64	F.	R. 3rd toe	Infection	,,	4 years	,, ,,
31	77	F.	L. 3rd and 4th toes	,,	,,	1 year	Died (cerebral haemorrhage)
32	64	M.	R. 2nd toe	Vascular	Amputation	2½ years	Satisfactory (ambulant)
33	53	M.	R. great toe	Infection	Local	5 ,,	,, ,,
34	60	F.	R 3rd and 4th toes	,,	Amputation	4 ,,	,, ,,
35	61	M.	L. 2nd toe	Vascular	,,	10 months	,, ,,
36	69	F.	R. great and 2nd toes	,,	,,	3 years	,, ,,
37	72	F.	L. plantar	,,	Local	1 year	,, ,,
38	64	F.	L. 5th toe	Infection	Amputation	1½ years	Died (coronary occlusion)
39	55	M.	R. 1st interosseous	Infection (fungus)	Local	5 ,,	Satisfactory (ambulant)
40	49	F.	R. great toe	Paronychia	,,	2 ,,	,, ,,
41	60	M.	L 2nd and 3rd toes	Vascular	Amputation	5½ ,,	Satisfactory (L. hemiplegia)
42	68	F.	R heel	Infection	Local	1½ ,,	Satisfactory (ambulant)
43	54	F.	Dorsum L. foot	,,	,,	2 ,,	,, ,,
44	59	F.	L. 1st toe	Vascular	Amputation	2 ,,	,, ,,
45	57	M.	L. great toe	Infection	Local	8 months	,, ,,
46	63	F.	L. 2nd toe	,,	,,	1 year	,, ,,
47	62	F.	R 4th and 5th toes	Fungus and vascular	Amputation	1½ years	,, ,,
48	68	M.	R 2nd toe	Infection	,,	3 ,,	,, ,,
49	71	F.	R 3rd and 4th toes	Vascular	,,	1 year	Satisfactory (R. hemiplegia)
50	62	F.	L. great toe	Infection	,,	2 years	Satisfactory (ambulant)

FIG. 1.—Case 1.

ether. Penicillin administered intramuscularly. Wound granulated satisfactorily and patient discharged after 19 days. *X*-ray film of foot showed "gross arthritic changes with some joint erosion."

Patient readmitted July, 1950, on account of persistent aching and discoloration of the right third toe. *X*-ray picture was essentially the same as that noted one year previously. The affected toe was removed under general anaesthesia; the wound healed satisfactorily and the patient was discharged after 15 days. She has had no further trouble, and is able to walk unaided (see Fig. 1).

Case 2

A woman aged 61. Diabetic for 15 years, taking soluble insulin, 15 units twice daily. Admitted February, 1949.

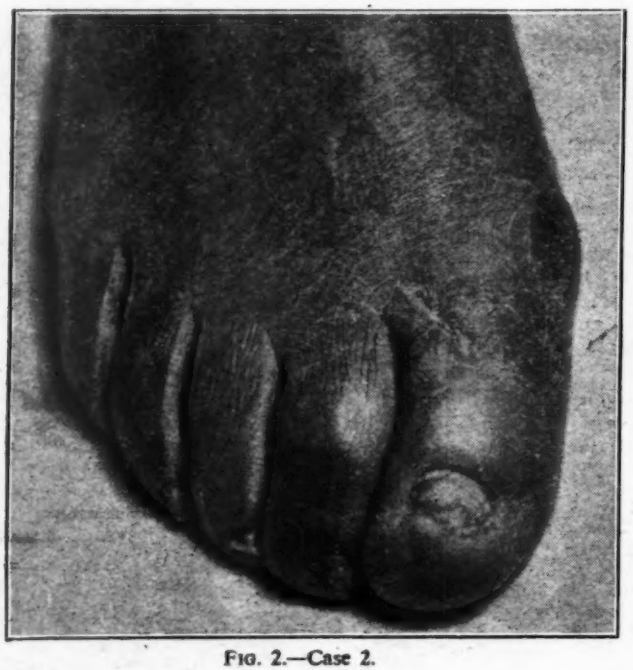

FIG. 2.—Case 2.

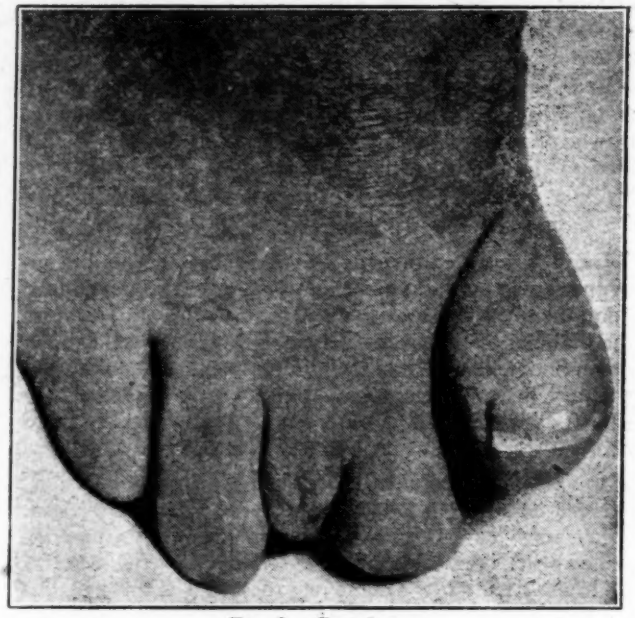

FIG. 3.—Case 3.

Gangrenous tissue present on the plantar and dorsal aspects of the right great toe with underlying pus. Blood pressure 150/90. There was a marked varicose eczema of the right calf. *X*-ray picture showed "a little decalcification of the bones of the foot, and calcification of the arteries, but no evidence of bony necrosis." The area was laid open, cleansed with hydrogen peroxide and methylated ether, and dressed with tulle gras. Improvement in this case was rather slow and was interrupted by a localized pocketing of pus; this was drained, and the wound healed satisfactorily. Free bleeding occurred when the tissues were incised, and the prognosis was regarded as good (see Fig. 2).

Case 3

A woman aged 70. Diabetic for two and a half years, taking 6 units protamine zinc insulin daily. Admitted August, 1949, with redness and swelling of right great toe. *X*-ray picture showed "bony necrosis in the region of the interphalangeal joint."

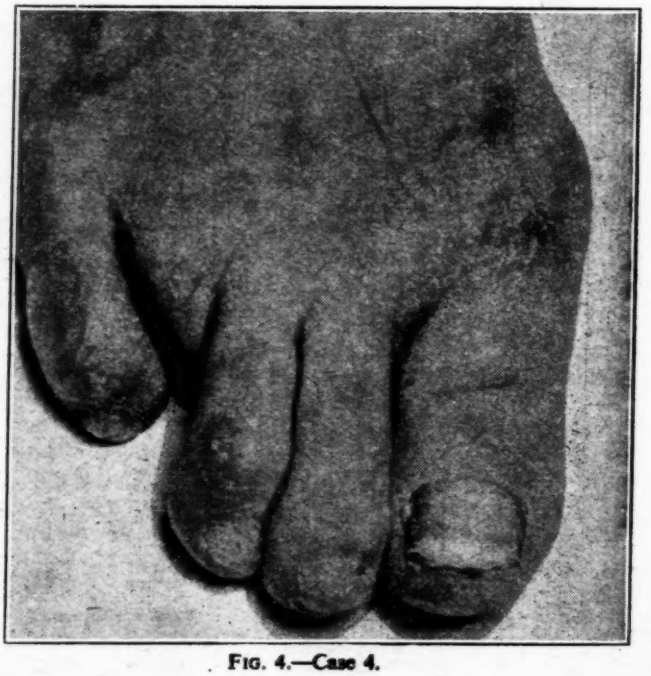

FIG. 4.—Case 4.

Procedure.—Removal of base of first phalanx and head of first metatarsal, right foot. The metatarsal head was found to be necrotic. Recovery was uneventful, and the patient was discharged a few weeks later. In December, 1949, the adjacent second toe was amputated because of necrosis of the terminal phalanx.

Readmitted January, 1950, with redness and swelling of the second left toe. *X*-ray film showed "necrosis of the tip of the terminal phalanx." Local amputation of the affected digit was carried out under general anaesthesia. There has been no recurrence, and the patient can walk about unaided (see Fig. 3).

Case 4

A woman aged 47. Diabetic for five years, taking 20 units protamine zinc insulin and 10 units soluble insulin daily. Admitted February, 1950, with swelling and inflammation of the fourth right toe and lymphangitis of the dorsum of the foot. *X*-ray film showed "erosion of the middle phalanx." Systemic penicillin was administered and the inflammatory condition subsided. No surgical intervention was advised at that time.

Readmitted May, 1950, with recurrence of pain and swelling in the same toe.

Procedure.—Removal of the affected toe under general anaesthesia. Good functional result, and no evidence of recurrence since discharge (see Fig. 4).

The first three patients had all been advised elsewhere to have amputation performed, either of the foot only or at a higher level. All of them are still fully ambulant despite the loss of one or more toes.

Discussion

Are not these results in contrast with those obtained in non-diabetic senile gangrene, which almost inevitably necessitates above-knee amputation? It has been our experience that gangrene in the non-diabetic, even without thrombosis in the main vessels, has not been amenable to treatment by conservative surgery, which can give such encouraging results in the diabetic patient of comparable age. The question thus arises, Why should such a difference exist in patients of similar age and with a comparable degree of vascular degeneration where one is a diabetic and the other not?

The superimposed infection is currently believed to be the dominating factor in diabetic gangrene, and the good results of conservative surgery are attributed to the adequate control of the infection. It is our opinion, however, that the control of the infection is only a secondary factor, and we venture the suggestion that in the diabetic an adequate collateral circulation is already in existence.

It is known that diabetes mellitus predisposes to early degenerative changes in the intima of arteries, and various reasons for this have been suggested, such as increased blood cholesterol and high blood fat, but it is still open to question whether these theories provide the complete explanation. There is no doubt, however, that histological examination of the blood vessels of young diabetics often shows intimal proliferation with deposits of cholesterol crystals and lipid-containing cells. Joslin *et al.* (1946) quote Case 1305, a boy of 16, in whose aorta atheromatous plaques were found; similar findings in young adults are described by Smith (1925) and Oppenheimer and Fishberg (1925).

Joslin and his colleagues hold the view, and our own results support it, that the slowly progressive occlusion of the vascular lumen stimulates the development of collaterals in the limb. When, therefore, complete obstruction occurs in the smaller vessels, this collateral circulation maintains satisfactory nutrition in the neighbourhood. Control of infection in the affected toe, either by simple débridement and drainage or by local amputation, will prevent spread to adjacent parts and thus hinder thrombosis in vessels which are still patent.

On the other hand, the non-diabetic with senile medial sclerosis, who suddenly develops a thrombus in one of the large vessels, has no compensatory mechanism, and so widespread necrosis takes place below the level of the obstruction.

Summary

Gangrene in the diabetic is extremely amenable to conservative surgery, and a radical amputation should never be performed as a routine measure. The theory is advanced that, although control of infection of the gangrenous tissue is of paramount importance, the diabetic state stimulates the formation of a collateral circulation which is usually well established when the crisis of peripheral vascular thrombosis supervenes.

We should like to express our thanks to Professor A. M. Boyd, Department of Surgery, Royal Infirmary, Manchester, for his helpful criticism and encouragement in the preparation of this paper.

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ASSOCIATED PERFORATION AND HAEMORRHAGE IN PEPTIC ULCERS

TREATMENT BY IMMEDIATE GASTRECTOMY

BY

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While perforation and haemorrhage are both common complications of peptic ulceration, they do not, fortunately, often occur simultaneously. Gordon-Taylor (1937) has classified these associated disasters into three groups: (1) haemorrhage and perforation occurring concomitantly, (2) haemorrhage following a recently treated perforation, and (3) perforation occurring after haemorrhage.

I wish to report three recent cases which fall into the first group and in which the two complications presented together. Case 3 is unusual in the pathological findings.

Case 1

A man aged 40 was admitted as an emergency on May 22, 1950, having had a sudden onset of generalized abdominal pain six hours previously. He had vomited several times in the interval and brought up "coffee grounds." A five-year history suggestive of peptic ulceration was obtained, and clinically he presented characteristic features of a perforated peptic ulcer. In addition he was very shocked and showed marked pallor. His blood pressure was 100/? mm. Hg, the radial pulse was of poor volume, and the peripheral circulation showed signs of collapse. A Ryle's tube obtained altered blood from the stomach. Pre-operatively 2 pints (1.14 litres) of blood was given followed by plasma, and two hours later his general condition had improved, his blood pressure rising to 120/90 mm. Hg.

At operation, under general anaesthesia, a perforated ulcer was found on the antero-superior aspect of the first part of the duodenum. The peritoneal cavity was full of

blood and exudate, the former being seen to come from the perforation. A gastrectomy, removing the ulcer, was performed with an antecolic Polya gastro-jejunostomy. The removed stomach and duodenum showed an extensive duodenal ulcer, which had eroded into three large branches of the right gastric artery, their open mouths being visible in the floor of the ulcer.

The immediate post-operative convalescence was uneventful, but seven days after operation a remittent fever and physical signs at the right base suggested a developing subphrenic abscess. Screening of the chest showed no movement of the right cupola of the diaphragm. He was given penicillin systemically and 2 further pints (1.14 litres) of blood. Within a week there was a marked clinical improvement, and the pyrexia subsided. When the chest was screened again 10 days later diaphragmatic movement was found to be full. The patient was discharged symptom-free and eating well on June 15. When subsequently seen in the "follow-up" clinic his progress was maintained; he had returned to a normal diet and had had no further indigestion.

Case 2

A man aged 52 was admitted as an emergency on October 10, 1950, having had a sudden onset of generalized abdominal pain four hours previously. He had vomited once and brought up "coffee grounds." A history of peptic ulceration covering 10 to 15 years was obtained, but there was no suggestion of previous haemorrhage. Clinically he presented the classical signs of a perforated peptic ulcer, and was not unduly shocked or pale. His blood pressure was 140/100 mm. Hg. A Ryle's tube obtained altered blood in moderate quantity from the stomach.

At operation, under general anaesthesia, a perforated ulcer was found on the antero-superior aspect of the first part of the duodenum, through which poured altered and fresh blood. A high gastrectomy was performed with an antecolic valvular anastomosis. The excised stomach and duodenum showed a duodenal ulcer which had eroded a large branch of the right gastric artery. During and after operation he received 2 pints (1.14 litres) of blood. His post-operative convalescence was quite uneventful, and he was discharged on October 24. When seen in the "follow-up" clinic he looked extremely well and was on a normal diet and free of dyspepsia.

Case 3

A man aged 60 was admitted on October 29, 1950. He had a history of sudden severe abdominal pain which had come on eight hours previously. He had twice vomited fresh blood before admission and brought up a further 8–12 oz. (230–340 ml.) of bright blood in the receiving-room. There was a history of indigestion covering a period of several years and a possible melaena stool 12 hours before admission. On examination his abdomen showed signs typical of a perforated peptic ulcer. In addition he was very pale and shocked, his blood pressure being 70/50 mm. Hg. An immediate transfusion was begun, and within two hours his blood pressure had risen to 100/75 mm. Hg, with considerable clinical improvement. He was then considered fit for operation.

Photograph of stomach resected from Case 3. The highest of the three gastric ulcers was bleeding and the duodenal ulcer had perforated.

Laparotomy, under general anaesthesia, showed a perforated ulcer on the antero-superior aspect of the first part of the duodenum, from which poured considerable quantities of altered and fresh blood. Routine palpation of the stomach revealed the presence of a large gastric ulcer high on the lesser curvature, firmly adherent to the pancreas. It appeared possible, therefore, that a gastric ulcer was responsible for the bleeding. A high gastrectomy was performed, with an antecolic Polya gastro-jejunostomy. Ligation of the left gastric vessels presented some difficulty, as they were involved in the ulcer bed. The specimen removed (see illustration) showed that there were, in fact, four ulcers: a large high lesser-curve ulcer eroding a branch of the left gastric artery, this being responsible for the haemorrhage; two smaller shallow ulcers on the lesser curvature; and a perforated duodenal ulcer.

The immediate post-operative convalescence was uneventful, but five days after operation the urinary output diminished in spite of adequate fluid intake and attention to electrolyte balance. The patient finally became anuric, dying on the ninth post-operative day with a blood urea of 375 mg. per 100 ml. Necropsy showed generalized oedema, marked in the lungs, and the kidneys had a mottled, pale, swollen cortex. On section these showed the histological appearances of a "lower nephron nephrosis." These changes could have been caused by a period of kidney anoxia due to the gross anaemia resulting from the recent severe blood loss, and by shock with a blood pressure little over 70 mm. Hg for several hours before operation. The site of operation appeared satisfactory.

Discussion

There is an axiom which states, "Bleeding peptic ulcers do not perforate, and perforated ulcers do not bleed." Anatomical reasons for this in duodenal ulcers have been advanced, and an anaemic spot has been described on the anterior aspect of the first part of the duodenum, where most such ulcers occur (Einhorn, 1930). However, in most reviews of peptic ulceration complicated by perforation 20% of cases give a previous history of bleeding. Further, the double complication is said to occur in between 1 and 3% (Baker, 1947; Gordon-Taylor, 1937) and 13% (Olson and Norgore, 1946). The lower figures would probably be more representative of experience in this country.

I have found no reference in recent American or British literature to concomitant bleeding in one peptic ulcer and perforation of another, though Kaye (1946) describes perforation of a pre-pyloric ulcer and six days later a fatal haemorrhage from a chronic high lesser-curve gastric ulcer. There is a similarity between his case and Case 3, the difference in the timing of the two complications being probably fortuitous. In addition, the two uncomplicated ulcers of the lesser-curve make Case 3 an unusual one. It is interesting to note, in passing, that neither of these two gastric ulcers was palpable at operation, being discovered only on examination of the excised stomach. In operating for a suspected bleeding peptic ulcer, the absence of external indication or palpable evidence should not, therefore, too easily deter the surgeon (Ives, 1949), nor should it be too hastily assumed that an obvious ulcer is necessarily the one causing the haemorrhage. It is by no means uncommon, on examination of "cold" gastrectomy specimens, to find

evidence of associated gastric and duodenal ulcers, or multiple lesions in the stomach or duodenum.

Gordon-Taylor (1937), in his classical review of the part surgery may play in the treatment of bleeding peptic ulcers, divides the problem of associated haemorrhage and perforation into the three groups mentioned above. He points out the great difference in prognosis between those cases in which the bleeding occurs at the same time as perforation (group 1) and of those in which either of the two complications occurs during recovery from the other (groups 2 and 3). He was able to quote five personal cases in the first group with no mortality. Four of these involved gastric ulcers and one a duodenal ulcer.

Where haemorrhage arises from an ulcer which has recently been sutured for perforation (group 2) all authorities agree that medical measures should be pursued, and, though such haemorrhage is a complication of the most calamitous nature, recovery does sometimes take place.

Where perforation has complicated a bleeding peptic ulcer (group 3) operation is indicated, though a large proportion of cases are not fit for any form of surgery. Gordon-Taylor (1937) states that he has never seen a recovery with or without operation. In a later paper (Gordon-Taylor, 1946) he quotes Avery Jones, who regards severe pain before, and particularly when it persists after, haemorrhage as a point of bad prognostic significance and a possible indication for surgical intervention. The diagnosis of perforation may be difficult in a shocked exsanguinated patient. If an early perforation is not to be missed, surgical treatment, where the patient can be made fit for it, would therefore seem urgently indicated when ulcer pain persists after haemorrhage.

Summary

The subject of associated haematemesis and perforation in peptic ulcers is reviewed. Three cases are presented in which the double complication occurred simultaneously.

Treatment by immediate gastrectomy is discussed.

I should like to thank Mr. Frank Forty, under whom these cases were admitted, for allowing me to operate on them and for the encouragement and stimulating advice he has given both in the management of the cases and in making this record. I am grateful to Miss N. H. Shaw, who is responsible for the photography.

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At a joint meeting of psychiatrists and chest physicians held by the Royal Medico-Psychological Association and N.A.P.T. on November 15 Dr. Andrew Morland discussed the reasons why the incidence of tuberculosis in mental hospitals was seven or eight times that in the general population. He said that although the chances of infection were greater, he felt that the lowered resistance of mental patients due to fears and depressions was a more likely cause. Dr. R. G. Maclaren thought that with mental patients the three chief evils were overcrowding, particularly at night, the grave shortage of nurses, and the low standard of dietary. Also patients sometimes refused to eat and needed much individual attention to get them to do so. Dr. B. T. Mann pointed out the risk to the community at large owing to the high proportion of mental patients discharged each year. Dr. Freida R. Hendeles described the organization of a tuberculosis unit in a mental hospital, and advocated a bed provision of 2½% of the total beds to be served.

BRONCHIECTASIS WITH UNSUSPECTED FOREIGN BODY

BY

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Four cases of bronchiectasis admitted to one chest hospital during the last six years, and treated by resection, were found to have an entirely unsuspected intrabronchial foreign body in the portion of lung removed. In none of them was there any history to suggest the inhalation of a foreign body, even on direct questioning after operation.

Case 1

An unmarried woman aged 22, of no occupation, was admitted on January 15, 1948. She had had pneumonia with haemoptysis in 1945. A further haemoptysis occurred in 1946 (a cupful), and another in 1947, when the severity demanded a blood transfusion. Between these attacks and her admission she had no complaints.

On examination the patient appeared to be a normal healthy young woman. Her weight was 9 st. 2 lb. (58 kg.). temperature 98.4° F. (36.9° C.), pulse 90, and blood pressure 114/80. Air entry was impaired in the left upper zone of the chest. Repeated sputum examinations revealed a mucopurulent trace, but no tubercle bacilli. A blood count showed: red cells, 4,000,000; haemoglobin, 80%; white cells, 9,000. A chest radiograph showed a slight increase in striation in the left lower zone. Bronchoscopy revealed only mucopurulent secretion from the left upper lobe orifice. Bronchography showed lingular and left anterior bronchiectasis; the remaining branches were normal.

Operative treatment was indicated by repeated haemorrhage, and on March 4 resection of the affected lingular and left anterior segments was successfully performed. The post-operative course was satisfactory, and she was discharged on March 13. A follow-up report by her doctor stated that she was well and free from respiratory symptoms.

Examination of the specimen showed bronchiectasis with infection and fibrosis affecting the lingular and left anterior bronchi. Within the bronchus was a mass of inspissated material containing vegetable seed cases and stalks. Microscopical section showed considerable submucosal infection with spherical hyaline bodies, probably also of vegetable origin.

No history was obtained before or after operation of an incident in which the grass seeds might have been inhaled, but on direct questioning after operation the girl's mother said that as a child the patient would often chew stalks of grass.

Case 2

An unmarried woman, a houseworker aged 32, was admitted on December 30, 1947. In May, 1947, dental extractions were carried out under general anaesthesia. A few weeks later she had a cough with foul sputum, occasionally streaked with blood, and in October she was treated for lung abscess with penicillin and postural drainage. Up to the time of admission she still had a cough with a little purulent sputum.

On examination she appeared to be a healthy woman. Her weight was 6 st. 2 lb. (39 kg.), temperature 98.4° F. (36.9° C.), and pulse 80. Her sputum was fetid, purulent, up to ½ oz. (14 ml.) in quantity, and contained no tubercle bacilli on repeated examination. Chest examination revealed impaired movement and air entry with occasional added moist sounds in the right upper zone anteriorly. Her blood pressure was 120/70, haemoglobin 100%, white cells 16,000. A chest radiograph revealed a streaky opacity in the right anterior region, and a dilated bronchus could be seen in the

postero-anterior view. Bronchoscopy showed only pus in the right upper lobe orifice. Bronchography revealed bronchiectasis of the right anterior segment, the anterior part being a little worse than the axillary.

Operative treatment was indicated by the persistence of symptoms in spite of conservative treatment, and on January 20, 1948, the right anterior segment was excised. Convalescence was entirely satisfactory, she was discharged on February 15, and at a later follow-up attendance she was well and without symptoms.

Examination of the specimen revealed a plug of interwoven hair in the anterior bronchus. Section of the bronchus showed that the epithelium had undergone metaplasia to the squamous type. The squamous epithelium showed no hair follicles or secretory glands. The hairs themselves were of various colours. They showed no root structures and appeared to have been cut at both ends. Considerable maceration had occurred, and identification of animal type was not possible. The rest of the segment showed changes of bronchiectasis and infection.

Case 3

A builder's buyer aged 28 was admitted on March 25, 1950. In May, 1941, he had a submucous resection of deflected nasal septum under local analgesia to become eligible for air duties, and later joined the R.A.F. He was quite fit until December, 1941, when he had a 4-oz. (114-ml.) haemoptysis. While this was being investigated in hospital he developed a right-sided pneumonia and right basal empyema for which a rib resection was necessary. He was discharged from the Service, and a year later he had a left basal empyema, which was also drained. This cleared completely, and he was free from symptoms for the next five years. In 1948 he developed a productive cough with about 2 oz. (57 ml.) of offensive sputum daily which continued up to the date of admission. There was no frank haemoptysis, but the sputum showed occasional pink staining.

On examination the patient was seen to be a heavily built man. His weight was 13 st. 5 lb. (85 kg.), temperature 98.4° F. (36.9° C.), and pulse 70. The chest showed bilateral healed empyema wounds. In the left lower zone were multiple coarse moist persistent rales. His blood pressure was 140/90. A chest radiograph showed increased left basal markings. Bronchograms showed gross lingular and left lower lobe bronchiectasis of cylindrical type. Other bronchi appeared quite normal.

He had been conducting postural treatment himself for some months before admission, but symptoms remained, and he regarded his cough and offensive sputum as a severe disability at work. Operative treatment was therefore indicated, and on April 11 left lower lobectomy and lingulectomy were performed. Convalescence was uninterrupted; he was discharged on May 4, and has remained well.

The specimen showed fairly severe bronchiectasis with infection and fibrosis in the lingula and basal segments of the lower lobe. The attached lymph nodes were markedly enlarged. In the section there was one bronchus lined by acutely inflamed granulation tissue which contained a minute foreign body, probably a spicule of bone, which was undergoing absorption.

Case 4

A housewife aged 28 was admitted on May 31, 1944. She had been well until January, 1943, when she developed right-sided pneumonia and subsequently an empyema. The latter was treated first by aspirations and then by rib resection and drainage for 11 weeks. The sinus quickly healed and she became well. In February, 1944, she had a haemoptysis of half a pint (284 ml.), and there was repeated blood-staining of the sputum.

On examination she appeared to be a normal healthy woman. Her weight was 10 st. 2 lb. (64.5 kg.), and her temperature and pulse were normal. Chest examination revealed a healed empyema scar at the right base. There was limitation of movement of the whole right side, with impaired percussion note at the base; coarse rales were audible at the base, back, and front. There was a trace of blood-stained, but not foul, yellow sputum. A blood count showed: white cells, 10,000; red cells, 5,250,000; haemoglobin, 92%. A chest radiograph revealed no abnormality except old lipiodol in the lung fields and deformity of the right ninth rib from old resection. Bronchography showed: right side, rather irregular bronchiectatic cavities of the saccular type throughout most of the lower lobe; middle and upper lobes completely clear; the left bronchial tree was normal. Bronchoscopy was not performed until immediately before operation. Nothing unusual was noted.

Operative treatment was selected, and on June 1 a right lower lobectomy was performed. Convalescence was complicated by an empyema which required drainage, and there was a small bronchopleural fistula present for a time, but she was well when discharged on October 10, and has remained so up to the time of her last follow-up attendance in September, 1950.

The specimen showed bronchiectasis of the posterior basic bronchus with bulbous dilatation of the peripheral end. This contained a large plum-shaped piece of granulation tissue and alongside it an elongated piece of cancellous bone, 6 mm. long. A section of the dilated end of the bronchus showed mucosa infiltrated with leucocytes and a mass of granulation tissue arising from it.

Discussion

In none of the cases described was any history obtained to suggest the presence of a foreign body. Case 3 showed a particularly small foreign body with apparently disproportionately extensive bronchiectasis, and there is no means of proving that the inhalation of the piece of bone occurred before rather than after the development of bronchiectasis; but the history of a haemoptysis some six years before the development of a productive cough must be regarded as strongly suggestive of the primary inhalation of a foreign body and secondary bronchiectasis.

Haemoptysis marked the onset of the illness in Cases 1 and 3, and the relapse in Case 4. Blood-staining of the purulent sputum was often present in Case 2. Thus in all four cases haemoptysis was a marked symptom. In comparison, only 42 out of 100 typical bronchiectatic cases chosen at random from the hospital records gave a history of haemoptysis or stained sputum.

Summary and Conclusions

Four cases of bronchiectasis with unsuspected foreign body are reported.

Comparison with other cases of bronchiectasis does not show these to be clinically or radiologically distinct, but it is of interest that haemoptysis occurred in all of them and that none was bilateral.

A foreign body lying in a bed of granulations in a bronchus is likely to cause frank haemorrhage, and this may provide a clue to its presence.

The presence of an unsuspected foreign body must always be borne in mind when a case of bronchiectasis is assessed, and all operation specimens should be thoroughly examined to exclude it.

Routine bronchoscopy may not reveal the presence of a foreign body which is the cause of bronchiectasis.

I wish to thank Mr. T. Holmes Sellors and Mr. Vernon C. Thompson for permission to report these cases, and members of the staff of the London Chest Hospital who have helped me in the preparation of this paper.

Medical Memorandum

A Fatal Case of Still's Disease Complicated by Amyloidosis

The following case is that of a child who died from Still's disease and in whom evidence of amyloidosis was found at the post-mortem examination. This adds to the number of cases described by various writers recently, including Hill (1948), Jennings (1950), and Skelton (1951).

Case Report

A girl aged 12 years was admitted to hospital in September, 1948, suffering from rheumatoid arthritis, the sequel to an attack of acute rheumatism in January, when both wrists and both knee-joints were involved. A previous attack of acute rheumatoid arthritis had occurred in 1940, but between the two illnesses her health had been normal. In early childhood she had suffered from whooping-cough and measles, and tonsillectomy had been performed at the age of 2.

The patient was an undersized thin pale girl, and weighed 4 st. 3 lb. (26.8 kg.). The chest was poorly developed. There was no cardiac enlargement and the heart sounds were normal. The pulse rate was 100 and the blood pressure 136/86. The lower edge of the liver was palpable. There were stiffness and swelling of the right elbow-joint with limitation of extension, and swelling and reduction of movements were present in both wrist-joints. The knee-joints were enlarged and globular in outline and very stiff. An *x*-ray examination of the hands showed osteoporosis of the bones and diminution of the carpo-metacarpal joint spaces. The E.S.R. was 66 mm. in one hour (Westergren). The red cells numbered 4,300,000 per c.mm., and the white cells 7,800; the haemoglobin was 75% (Sahli). The urine was normal. In December, 1948, the E.S.R. was 70 mm., the liver was enlarged one fingerbreadth below the costal margin, and the spleen was palpable. There was no fever, and less pain was complained of in the affected joints.

In March, 1949, the joints became stiffer and more painful, and the E.S.R. was 110 mm. During the summer there was a gain of 4½ lb. (2 kg.) in weight, but in the autumn an exacerbation of joint symptoms took place, the liver and spleen showed further enlargement, and there was a sharp epistaxis in October. In November, 1949, generalized enlargement of the lymph nodes was noticed, and the blood count showed: red cells, 3,200,000 per c.mm.; white cells, 11,900; and haemoglobin, 7.7 g.% (Sahli). No albumin was noted in the urine. Several attacks of vomiting and a further epistaxis occurred in December, 1949, when her weight was 3 st. 1 lb. (19.5 kg.).

A lymph node was removed for histological examination and reported upon as follows: "There is follicular hyperplasia with amyloid infiltration in many of the germinal centres. The sinuses are filled with catarrhal cells and show also small haemorrhages and haemosiderin. In the medulla there are numerous clumps of polymorphs and plasma cells, but no organisms were seen. The appearances are considered to be not incompatible with findings reported in Still's disease."

During January, 1950, there were attacks of vomiting and diarrhoea. The plasma proteins were 7 g.% and the icteric index 7. The Takata-Ara test was weakly positive, and the thymol turbidity test gave 5 units. During February the patient became more feverish and suffered from attacks of epigastric pain and further diarrhoea, due to Sonne dysentery infection. Her condition steadily deteriorated, and death occurred on February 9, 1950.

Post Mortem.—The body was that of an undersized and extremely emaciated child. Movement of the limbs and head was limited by arthritic changes. Some enlarged lymph nodes could be felt, and there was a firm homogeneous mass in the upper part of the abdomen. The tongue, larynx, oesophagus, and trachea were extremely dry; the lungs were pale, and bound to the chest by numerous adhesions. No fluid was found in the pleural cavities. The hilar nodes were enlarged and elastic. The pericardial sac contained a small quantity of clear fluid. The heart was small and pale. No valvular defects were noticed, and the heart muscle did not give any reaction with iodine. The liver was very large and pale, and weighed 2,030 g. The cut surface had the appearance of amyloid after staining with iodine. The stomach was small, the mucous membrane pale. The small intestines were distended and purple, and contained blood and mucus. The large bowel presented a similar appearance. The kidneys were small and gave the reaction for amyloid. The suprarenals were large and pale, and were considered to contain amyloid. The spleen weighed 230 g. and gave a doubtful amyloid reaction. The para-aortic glands were enlarged and of an indiarubber consistence, and the mesenteric glands were dark in colour.

Discussion

The most pronounced amyloid changes were found in the liver, kidneys, suprarenals, and lymph nodes. The persistent vomiting, diarrhoea, and haemorrhage were important factors in bringing about the fatal termination. The urine was free from albumin throughout the illness. A certain degree of anaemia was present in November, 1949, and, since the blood picture suggested malabsorption as the cause, the patient was treated with liver. The value of liver therapy in amyloidosis has been shown by Grayzel and Jacobi (1938), but benefit is not invariable, and in this case the treatment was not effective. Reimann and Eklund (1935) state that amyloidosis appears only after a protracted illness, and that all the cases described have been emaciated and anaemic. Death in this particular case was due to terminal dysentery, and the amyloidosis was not by itself responsible. It was evident that the rheumatic process was never properly arrested—a fact which no doubt prevented regression of the amyloid changes.

Recovery from this condition has been noted by Trasoff *et al.* (1944), who have found albuminuria present in nearly all the described cases. Carroll and Nelson (1927) emphasize the gravity of its occurrence and say that it is always preceded by severe or moderately severe arthritis of some duration. Hill (1948) states that most of the published cases refer to children. It is suggested that in the present case the amyloid changes found in the liver, kidneys, and lymph nodes were due to the rheumatic infection and that the numerous pleural adhesions were also probably of rheumatic origin, since no evidence of tuberculosis could be found in the body at necropsy.

I am indebted to Mr. R. V. Liddell for biopsy of the lymph node; to Dr. E. J. M. Shearer for the details of the post-mortem examination; and to Dr. D. A. Leslie, of the Department of Pathology, University of St. Andrews, Dundee, for the histological report on the lymph node.

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Reviews

TEXTBOOK OF PAEDIATRICS

Disease in Infancy and Childhood. By Richard W. B. Ellis, O.B.E., M.A., M.D., F.R.C.P. (Pp. 696; 300 illustrations. £2 2s.) Edinburgh: E. and S. Livingstone. 1951.

Professor R. W. B. Ellis has done a fine piece of work in writing this book. It is a large volume of 680 pages, and is planned to guide the reader along the common-sense approach to paediatrics—namely, the path of developmental progress. After an introductory reference to history-taking and clinical examination the author discusses constitutional and environmental factors in disease, prenatal infections, congenital malformations, and the disorders of the newborn baby. Then follow accounts of abnormal conditions associated with nutrition and of growth and development during infancy and childhood. Subsequent chapters, though not rigidly systematic in the traditional textbook sense, are sometimes devoted to systems (blood, genito-urinary) and sometimes to pathological conditions—for instance, neoplastic disease, allergy, and tuberculosis. There is also a chapter on communicable diseases and another on behaviour disorders. The book ends with a description of some procedures common in paediatrics, such as transfusion.

Professor Ellis writes well, and his wide experience of paediatrics, both in this country and abroad, is presented in attractive and convincing style. He carefully considers the interdependence of the various facets of life—physical, intellectual, and emotional—and the reader is left in no doubt that the author's main concern is with the child as an individual. This surely is the right approach in an introduction to clinical paediatrics, as the author himself describes his book. But it is questionable whether the requirements of both undergraduates and postgraduates can be met within a single volume. For instance, the chapter on congenital malformations (120 pages) is admirable for postgraduates, but it might well be abbreviated for the student. And the pages saved in this way could profitably be used to elaborate other important subjects, such as the details of breast-feeding, the psychological problems of lactation, and the part played by the sense organs, especially the eyes and ears, in development during childhood. Nevertheless Professor Ellis has gone a long way towards providing the undergraduate reader with the essential background against which the child must be viewed if his illnesses are to be understood and prevented; for in the earlier years of life the beginnings of disease are to be found in the child's home and school, in the quality of his milk and food, in the social and economic circumstances of his life, in the health and wisdom of his parents, and in many other factors that often receive little more than lip-service in the textbooks.

The volume is well produced and includes nearly 300 illustrations. The index could usefully be made more comprehensive. The excellence of the paper makes the book heavy to hold, but it would be unreasonable to complain of this. One can only hope that the child mentioned on p. 314, who manufactured his gastric paper ball by regularly devouring the *Scotsman*, was cured of his habit before Professor Ellis's book became available as a temptation.

N. B. CAPON.

PROTHROMBIN

Prothrombin Deficiency. By Rosemary Biggs, M.D. (Pp. 84; 14 figures. 10s. 6d.) Oxford: Blackwell Scientific Publications. 1951.

The introduction of anticoagulants has focused attention on the laboratory assay of prothrombin activity in the blood of cases treated with such drugs. This practical application has stimulated many investigations into the chemistry of coagulation, so that during the past ten years a vast literature has developed on the subject. Dr. Biggs has tried to reduce the bulk of this literature into the compass of a short monograph. She has therefore had to pass over some of the still highly controversial points, but nevertheless she has presented the main problems clearly and concisely.

The book may be regarded as a supplement to the ordinary laboratory manual. The more usual techniques for estimating prothrombin activity are briefly and critically discussed, and the differing scopes of the one- and two-stage methods are clearly pointed out. The section on the investigation of cases of hypoprothrombinaemia of unknown aetiology is of practical value. The procedures used in the various tests are given in the appendices.

This book will be of use to the trainee in pathology who wants to obtain a basic knowledge of the "prothrombin question." Its 90 references to original articles present a good cross-section of the work now available and should make it easy to read more fully on the controversial aspects of the part played by prothrombin in the coagulation process. It will be a useful reference book in the routine clinical pathological laboratory.

H. PAYLING WRIGHT.

THEORIES OF EVOLUTION

Animal Evolution. A study of Recent Views of its Causes. By G. S. Carter. (Pp. 368; 63 figures. £1 10s.) London: Sidgwick and Jackson. 1951.

Dr. Carter's book is a valuable synthesis, summarizing the results obtained by the various different approaches to the problem of evolution and combining them to give a coherent picture of its causes. It is intended chiefly for the student reading zoology at a university, but its perusal will be found a stimulating experience by anyone whose main concern is with some other branch of animal biology and who wishes to refresh his ideas on evolution. The emphasis throughout is on the developments of the last thirty years.

The book is divided into two parts of about equal length. In the first ("The Basis of Biological Fact") the author discusses in turn the several approaches—the palaeontological data, the genetic background, the problems of species and of the various infra-specific categories, and the mathematical and experimental study of natural selection. In the second ("The Theory of Evolution") he is concerned with more general problems and discusses their theoretical explanation.

Dr. Carter distinguishes throughout between micro-evolution on the one hand—"the early stages of the evolutionary process in which differentiation begins and is built up to the specific stage of divergence"—and the larger changes of macro- and mega-evolution on the other. The first can be studied both palaeontologically and on living populations, the other two in the fossil record only. His theoretical part begins with micro-evolution, and he emphasizes the fact that the

discontinuous nature of the environment generally leads to the breaking up of the species into smaller interbreeding units of varying size, permanence, and isolation, which are termed "demes." This idea is of great importance, because, as he so clearly shows, the demes are the units which undergo evolutionary change. If they are small enough (as apparently they often can be) they may show non-adaptive evolution. "The earliest stages of differentiation take place in these partially isolated local populations, and from these beginnings the whole of micro-evolution is built up."

He turns from micro-evolution to the larger evolutionary changes, and after discussing allometry and aristogenesis, pre-adaptation, evolutionary trends, recapitulation, and finally the rate of evolution, he draws the conclusion that macro- and mega-evolution can be interpreted, largely at least, as due to the operation, for long periods of palaeontological time, of the same processes which work in micro-evolution. The time factor allows new aspects of the evolutionary process to become evident. He concludes by re-examining some of the classical objections to the Darwinian theory in the light of recent advances in knowledge.

G. P. WELLS.

THE TWO CATS

Wisdom, Madness, and Folly. The Philosophy of a Lunatic. By John Custance. Foreword by Canon L. W. Grensted. (Pp. 254. 16s.) London: Victor Gollancz. 1951.

The author does himself a serious injustice in giving his book the subtitle, "The Philosophy of a Lunatic." In fact he is not a lunatic, although he has had periods of lunacy—that is, typical and severe attacks of both mania and depression. He describes these episodes with clarity and feeling, so that they rank highly among the self-descriptions of psychotic patients. For that reason alone the book is interesting to the psychiatrist, and should be interesting to others too. In his case not only were the depressive phases a kind of Hell, but the manic phases, as is much less common, seemed very near to Heaven. Mr. Custance is naturally a deeply religious man, and the psychological necessity arose to try to relate his abnormal experiences with his religion and philosophy. He feels that they have enriched his mental and spiritual life, and would not now be without them, despite the distress they caused. The philosophy to which he is led emphasizes the objective reality of his experiences, and is indeed a form of idealism. Suppose he were to see, he says, in a hallucination a cat sitting next to him, he would be unable to distinguish the hallucinatory cat from a real one, and for his psychophysical system the two would be the same. In his "Theory of Actuality" no difference is made.

Mr. Custance's philosophical system, which is quite sane, will make a strong appeal to those who are attracted to idealist philosophies, but it will not do as the basis for a scientific approach. The reconciliation which he has found it to give between religion and science would be a shaky one. The trouble is that, if others were to deal with Mr. Custance's two hypothetical experiences, normal visual perception and hallucination, as equivalent, they would make practical errors of considerable consequence. A very successful method of helping the chronically hallucinated patient to get by in ordinary life consists in teaching him to distinguish, perhaps by adventitious circumstances, the hallucinated from the real, and to react differently to them.

In one mental hospital Mr. Custance experienced, as he credibly claims, a degree of brutality from the male nurses which would be a disgrace to any decently run institution; and, it is said, the doctor to whom he complained turned a blind eye. This distressing history is confined to an appendix, which, however, should be carefully read by psychiatrists. Such affairs are increasingly less likely to occur as a therapeutic rather than a custodial attitude develops in mental institutions. What Mr. Custance has to say about the way in which sympathy or antipathy may be aroused in the psychotic patient by the attitude of his doctors is of real value. He has, in fact, many practical suggestions to offer, such as the provision of incentives in occupational therapy, which could well be considered by hospital psychiatrists.

ELIOT SLATER.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The English Herbal of Physical Plants. By J. Pechey. (Pp. 96. 3s. 6d.) London: Hutchinson. 1951.

Antibiotics. By Sir Howard Florey, F.R.S., M.A., Ph.D. (Pp. 35. 6s.) Oxford: Blackwell Scientific Publications. 1951.

We of Nagasaki. By T. Nagai. (Pp. 207. 10s. 6d.) London: Victor Gollancz. 1951.

Parasitic Infections in Man. Edited by H. Most, M.D. (Pp. 229. 30s.) London: Geoffrey Cumberlege. 1951.

Metabolic Methods. By C. F. Consolazio and others. (Pp. 471. 48s.) London: Henry Kimpton. 1951.

Instruments and Apparatus in Orthopaedic Surgery. By E. J. Nangle, M.B., Ch.B., F.R.C.S. (Pp. 231. 42s.) Oxford: Blackwell Scientific Publications. 1951.

Eosinophilic Lung. By T. J. Danaraj, M.D. (Pp. 57. No price.) Singapore: Papineau Studios, 304-U, Orchard Road. 1951.

Twenty-fourth Meeting of the Northern Surgical Association. Edited by E. Dahl-Iversen, M.D. (Pp. 365. No price.) Copenhagen: Ejnar Munksgaard. 1950.

La Philosophie de la Chirurgie. By Professor R. Leriche. (Pp. 251. 400 francs.) Paris: Flammarion. 1951.

The literature on nuclear physics has changed from a steady stream to a river in spate since the fission of the atom. Some of the work has been concerned with the application of radioactive isotopes to medical diagnosis and treatment, and with the biological and medical effects of high-energy radiations. As a key to this vast literature the United Nations Atomic Energy Commission published in 1949 Vol. 1 of its *International Bibliography on Atomic Energy.* It dealt with the political, economic, and social aspects of the subject. The Commission has now published a second volume (*An International Bibliography on Atomic Energy. Vol. 2. Scientific Aspects.* Atomic Energy Commission Group, United Nations, New York, 1951), which lists over 24,000 articles, books, and booklets published in all parts of the world between 1925 and 1949 on the scientific aspects of research in the field of atomic energy. The volume is divided into five chapters, of which Chapter 3 (on biological and medical effects of high-energy radiations) and Chapter 4 (on isotopes in biology and medicine) contain a total of 6,454 references. The book includes an author index and a list of abbreviations of journals cited. It is obtainable from H.M. Stationery Office, P.O. Box 569, London, S.E.1, price 75s. or $10.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY NOVEMBER 24 1951

CEREBRAL STRUCTURE AND PERSONALITY

Professor M. Bleuler's article in this issue will interest a wider circle of medical men than neurosurgeons, neurologists, and psychiatrists. Within the framework of a general discussion of great theoretical significance he brings out many points of everyday clinical importance. Among these are the facts that mental disturbance may be an early and distinctive sign that there is organic disease of the nervous system, and that structural changes in the brain may release symptoms of a neurotic or functional nature. The reciprocal relationship between brain lesions and changes in the personality and in emotional life is beginning to assume a central importance in psychiatry and in general medicine.

Another article published in this issue, that of Drs. A. A. Baker and L. Minski, adds to the evidence that neurosurgery has something to offer, and much to find out, in the treatment of chronic and intractable neuroses. But it is more than ever urgently necessary, as Professor Bleuler himself points out, that psychiatrists and surgeons should know what they are doing when inflicting a circumscribed cerebral lesion for purposes of treatment, and that their patients should not be subjected to useless surgical trials. This study from the Belmont Hospital, like many previous investigations, shows that no very consistent psychological defects result from leucotomy. The changes in the patients were on the whole beneficial, sometimes remarkably so; yet the authors say that they could be assessed only by their effect in the particular personality concerned. A given change might have a favourable effect in one patient and be less beneficial in another, and apart from the diminution of tension there was no very clear "post-leucotomy syndrome." An anterior cut causes a lesser and a posterior cut a greater degree of personality change, but qualitative differences between the two are not obvious. This is not very helpful for the surgeon wishing to improve operative technique. On this particular point Professor Bleuler, with the great experience gained by a planned psychiatric investigation of over 600 cases of cerebral tumour, is no more helpful, and indeed would go further and say that hope of obtaining definite information from such sources is founded on a misconception. The psychological symptoms which may help to locate the lesion are few indeed—from which it would seem to follow that there is little hope of designing special operations for the relief of specific symptoms.

This is not to say that the psychiatric study of organic diseases of the brain is not of great clinical importance. Symptoms of a psychological kind may be the first sign of such a disease and may be diagnostic of its existence. They are only likely to prove unhelpful when the question of location arises. Any one of three syndromes may be shown, depending on whether the lesion is acute or chronic, circumscribed or diffuse. In the acute lesion clouding of consciousness predominates. An amnestic syndrome will be found with chronic and generalized lesions. If the lesion is chronic and circumscribed there may be no psychiatric symptoms or only emotional changes of an uninformative kind. The most reliable localizing symptoms of a psychological kind—aphasia, apraxia, and agnosia—occurred in only 10% of Professor Bleuler's series, and would be considered more in the nature of neurological than psychiatric symptoms. Almost the same could be said of the uncinate fits, which are rarer and which Professor Bleuler found in about 3% of his cases. Major or minor epileptic fits were of practically no help in locating a lesion, though they were rare in cerebellar tumours. The famed "frontal syndrome," which is of special interest to psychiatrists, may just as often occur with a diencephalic as with a frontal lesion. Professor Bleuler does not fail to draw the general conclusions which are suggested by his work. An end can now be made of the long tradition, of which Kraepelin was a powerful advocate, demanding a search for specific diseases with specific syndromes attached to them. General paresis is a disease entity in the pathological sense, but its psychiatric effects may be indistinguishable from those of arteriosclerosis, alcoholism, or brain trauma. The only specific effects likely to be seen are in the colouring of organic pictures by features derived from the personality, as in the appearance of schizophrenic, manic-depressive, or neurotic signs. But when these are found they are no signposts to the affected part of the brain but only to the hereditary constitution.

Many neurologists and psychiatrists will read Professor Bleuler's views with strong sympathy. Excessively precise and detailed attempts to locate cerebral lesions unsupported by facts have been rightly stigmatized as "brain mythology." Yet the tendency to associate structure with function in the brain has persisted despite all disappointments, and

surely must still continue. The difficulties are extreme. Any disturbance in one part of the brain, especially an acute disturbance, is likely to upset function in all other parts. Specific signs are thereby obscured, but not necessarily put finally beyond the reach of research. One of the needless difficulties we have made for ourselves is to consider the problem from a too exclusively surgical and topographical standpoint. It is of the utmost importance to the neurosurgeon to decide whether a lesion is frontal or diencephalic. Anatomically there is a great difference, but functionally a much lesser one, for from the functional standpoint frontal cortex and diencephalon are so intimately connected as to form parts of the same system. It is conceivable that the effects desired by the psychiatrist when he asks for a leucotomy may be obtainable in future by an immensely delicate diencephalic operation, but totally inconceivable that the same effects will be obtained by operating on the parietal or occipital lobes.

THE M.R.C. AT WORK

In a report[1] issued this week the Medical Research Council reviews its work for the two years 1948–50. The main achievements of this period and an indication of the research on which they were based are described elsewhere at p. 1274. Financially, the Council has done its work with exemplary economy. In these two years the work has cost little more than £2½m., of which over half a million pounds was for non-recurring expenditure; few organizations spending public money can show such a low proportionate figure for administrative expenses, and fewer still such a record of useful achievement. In the financial year 1949–50 the M.R.C. spent 56% of its income on research units and external scientific staff, 23% on the National Institute for Medical Research, 11% on temporary research grants and training awards, and 4½% on administration; the remainder was spent on research on human factors in industrial productivity (4½%) and on general scientific purposes (1%).

From small beginnings in 1913, when it was known as the Medical Research Committee, the M.R.C. has grown into a large but close-knit and flexible organization. It can quickly deploy its resources and find the right man or team to study problems as they arise; likewise, when a particular task is completed, the M.R.C. can as soon withdraw and leave further development to clinicians, public health workers, or industrialists. The Council's strength has resided in its ability to organize research decisively, and in choosing the right people for any particular investigation.

[1] *Report of the Medical Research Council for the Years 1948-1950.* 1951. H.M.S.O., London.

Much of the M.R.C.'s growth took place immediately after the last war, when young men of promise were coming out of the Forces. Sir Edward Mellanby, then the Secretary to the Council, was quick to seize the opportunity, and during this period of active expansion many new research units were established. During the period reviewed in the present report two new units were set up: the Ophthalmological Research Unit at the Institute of Ophthalmology in London, and the Spectrographic Research Unit at the London Hospital. In addition the Council acquired the Antibiotics Research Station at Clevedon, in Somerset, for the production and investigation of promising new antibiotics; members of the external scientific staff were constituted as groups for research on chemotherapy (at Manchester) and on occupational optics (in London). In 1950 the National Institute for Medical Research was moved from Hampstead to more commodious accommodation at Mill Hill. The Council also undertook the staffing of the Royal Naval Tropical Research Unit, maintained by the Admiralty at Singapore; it assumed responsibility for the Ministry of Health Blood Group Reference Laboratory at the Lister Institute; and a new Division of Human Physiology was incorporated in the National Institute for Medical Research. This may seem to have been increase enough in two years, but in fact this period was one of consolidation while the Council adapted itself to the needs of peace from those of war. By the end of 1950, as well as the N.I.M.R. and the Antibiotics Research Station, the Council was directing 38 research units, 7 research groups, the Laboratory Animals Bureau, and a field research station in the Gambia. At this time its staff numbered 1,400; 450 were scientific staff, and 159 of these were medically qualified. The Council continued to administer the Public Health Laboratory Service on behalf of the Ministry of Health, and in this a further 855 staff were employed, of whom 134 were medically or scientifically qualified.

In the wise direction of this great effort different qualities are needed from those that the pioneers put to such good use. Dr. H. P. Himsworth, who succeeded Sir Edward Mellanby half-way through the period reviewed, has a delicate and difficult task to perform: he has a great organization to direct so that every worker in it benefits to the full from membership of the whole and does not waste his talents on ill-thought-out projects, yet at the same time each worker needs for his research that freedom of thought and imagination indispensable to creative work. The energies of good men can too easily be frittered away on time-consuming but second-rate investigations, sometimes most regrettably the

outcome of ill-informed political pressure. Waste of exceptional ability and training must at all times be resisted.

The publication of a two-year Report to Parliament is an occasion for taking stock. What does the work of the Medical Research Council contribute to medicine, and thus indirectly to the health of the nation? Apart from the immediate benefits due to new therapeutic substances, in the discovery of which M.R.C. workers are engaged, as are others elsewhere, the Council maintains establishments where long-term programmes of research may be pursued; a gifted man can afford to follow the intriguing bypath, and in this way more than one great discovery has come about. By means of grants and scholarships the Council supports many workers outside its own staff; these men, often at the outset of their careers, must surely benefit from this association, both from the advice and help so readily available to them and from the contact with men experienced in research. Again, the Council's statistically guided clinical trials have set a standard rarely seen in any other country, and they have done much to make therapeutics more rational, to correct widespread errors of opinion, and to indicate the best available remedial or preventive treatment. Lastly, the Council has intervened on occasions, as it did with effect during the war, to hasten the practical application of the discoveries of medical research. It used to be said that the time lag between a scientific discovery and its application was about a generation; that is no longer so in medicine in Britain, and much credit for the change is due to the M.R.C.

URGENT ADMISSIONS TO HOSPITAL

As the colder and shorter days of winter come upon us the weekly number of deaths in the great towns of England and Wales is increasing by about 5% over the previous week's total. Doctors with the memory of last winter fresh in their minds must feel some anxiety about the coming three months. And everyone should realize now that the great rush for admission to hospital comes in the weeks immediately after Christmas. An epidemic of influenza and an unusually high incidence of other infectious diseases last winter gave the Health Service a severe test, and many claimed that it failed to meet it. In its last annual report[1] the London Local Medical Committee stated it was appalled by the number of emergency cases which could not be got into hospital, and many doctors in Britain had the same experience. This committee discussed with the Ministry of Health the problem of getting patients admitted, and the General Medical Services Committee of the B.M.A. has also been active in making suggestions and asking for assistance. The Ministry has responded with a helpful circular[2] asking hospital boards and committees urgently to overhaul their arrangements for admitting the acutely ill and outlining a scheme for close co-operation between general practitioners and hospitals.

The first part of the scheme is concerned with communications between family doctor and hospital. Anyone supposing that the present telephone system provides adequate means of communication during epidemics would change his mind after spending a morning in a doctor's surgery—at least in many parts of the country. Telephone calls—to perhaps two or three hospitals for each case—being put through several times during 24 hours can waste a great deal of time urgently needed for examining patients or travelling to visit them. The doctor in his surgery or in a patient's house often cannot know with any certainty which particular hospital is the most likely to admit his patient, and the time he spends in finding out cannot be spared when the demands on his services are pressing. The pioneer work of the King Edward's Hospital Fund has shown how useful an emergency bed bureau can be in relieving general practitioners from the strain of fruitless telephonic inquiries. The success of the London Emergency Bed Service is widely acknowledged, and there are now many admissions bureaus of one kind or another throughout the country. In order to develop this kind of service the Ministry asks hospital boards to set up bureaus in any populous areas not yet covered by them. Many types of case will remain that are not suitable for referring to an admissions bureau because the family doctor considers that a particular hospital or a particular consultant is needed; in certain areas general practitioners prefer direct contact with the hospital and have no difficulty in getting their patients admitted: for such as these an admissions bureau is unnecessary—its use will not be compulsory. But in many towns, and especially during epidemics, admissions bureaus can greatly lighten the general practitioner's task by helping to admit the ordinary acute case into hospital.

The second important feature of the Ministry's scheme is to ensure that a responsible person is in charge of admissions to hospital. A complaint often heard since the Health Service started is that a hospital porter or switchboard operator has refused admission to an ill patient because the list in front of him showed that the beds were all occupied, whereas, had the decision lain with a doctor, he would somehow or

[1] *British Medical Journal Supplement*, May 19, p. 205.
[2] Ibid., November 17, p. 217.
[3] *British Medical Journal*, March 26, 1949, p. 532.

other have found room for the patient. The Ministry therefore proposes that every hospital with a resident medical staff should put one of its medical officers in charge of admissions. Hospitals without a resident medical staff must perforce put a lay officer in charge, but he should be of higher status than telephonist or porter. In every hospital management group, teaching and non-teaching, a group admissions officer is to be appointed; he must be at least a senior registrar, and preferably an S.H.M.O. or consultant. He is to be empowered to direct any hospital in the group to admit a patient. At a higher level an administrative medical officer on the regional board's staff will be responsible for assisting the group admissions officers.

These arrangements should go far to ensure that anyone in immediate need of a hospital bed will not be denied it. That the Ministry acted after the unpleasant and sometimes tragic experience of last winter instead of in anticipation of it is a matter for regret. The need for something like this in the Health Service should have been clear. As we said two and a half years ago,[3] "The most urgent need is for the quick re-establishment of authority to secure the immediate admission into a State hospital of an acutely ill person."

If these arrangements are to work successfully all concerned must be constantly exchanging information, and, as the Ministry points out, general practitioners can play an important part in providing hospitals with early information about prevalent sickness and forecasts of the likely demand for hospital beds. Too often are such schemes referred to as administrative machinery, as though they resembled some kind of machine that could be started up and left to run without much further attention. This one cannot work successfully during epidemics if wards are being painted in accordance with some decision taken perhaps a year previously and if admissions from waiting-lists are not carefully scrutinized. While the doctor's first concern is to treat his patient, medical men have a great opportunity here of ensuring that the patient is enabled to get the treatment he needs.

DISCIPLINE IN THE N.H.S.

Before July, 1948, many members of the medical profession were alarmed at the power given to the Minister to judge whether a general practitioner's conduct exposed him to punishment by fine and in particular to removal from the Service. The Minister of Health can dismiss from the N.H.S. any general practitioner on the ground that his continued inclusion would be "prejudicial to the efficiency of the service." Now that all but a small proportion of general practitioners are working in the N.H.S. such power in the hands of the Minister is the power to deprive a medical man of his livelihood. For this reason alone a review of the disciplinary machinery in the N.H.S. is called for, and the General Medical Services Committee is undertaking an investigation of it. Local medical committees have been asked to examine the machinery and to send in to the G.M.S. Committee any criticisms or suggestions that might be used as a basis for amending legislation.

Matters which come up for disciplinary discussion are over-prescribing, prescribing foods as drugs, and breach of terms of service. The local medical committee considers questions of over-prescribing and prescribing foods as drugs. It refers its recommendations to the local executive council. For considering what is more serious—an infringement of terms of service—there is set up in the area of each local executive council a medical service committee to which three lay members are appointed by the executive council and three medical members by the local medical committee; the committee itself elects a chairman from the lay members of the executive council. A patient having a complaint against a doctor must lodge it within six weeks of the causative event to the executive council; this time may be extended in exceptional circumstances. The proceedings are private, and doctor and patient can be helped to present their case by some other person, but neither solicitor nor barrister may conduct the case for either party by addressing the committee or by cross-examining witnesses. If the chairman of the medical service committee considers a complaint to be without proper grounds or to be frivolous or vexatious the committee, with due safeguards for the complainant, may report on the case without a hearing. In all cases the medical service committee must submit its report and recommendations to the local executive council, which must accept the facts as found by the committee and forward its report to the Minister with the council's own recommendations. The report and recommendations of both committee and council must be supplied to both parties to a dispute, who have the right of appeal to the Minister. The Minister must refer serious cases to the Tribunal. This consists of a chairman who is a lawyer, and two others—one appointed by the Minister after consultation with recognized associations of executive councils and one out of a panel of six persons chosen after consultation with the appropriate professional organization. The parties to this dispute may be represented by counsel or solicitor at the hearings before the Tribunal. Appeal against the findings of the Tribunal may be made to the Minister.

This in the briefest outline is the disciplinary machinery of the N.H.S. It must be asked whether the procedure provides for justice to be done in theory and in fact. If in theory the provision is such as would not satisfy a lawyer, are doctors and patients satisfied that, in general, justice in fact is done? The local mechanism for discipline is based on that used under N.H.I., and those with long experience of this usually

say that they were satisfied wi.. it. It is, however, easy to be misled by comparing conditions under N.H.I. with those under N.H.S., which in many respects are fundamentally different. Apart from the fact that the one was an insurance scheme and the other is not, there is the big difference that something like 95% of the public and of general practitioners are in the Service. For a doctor working in the N.H.S. to be dismissed from it amounts to being condemned to permanent unemployment. It is true that at every stage in the disciplinary process the respondent doctor's interests are watched over by his professional colleagues. Nevertheless a thorough examination of the disciplinary mechanism is necessary, for who knows what abuses of administrative power may creep in as the years pass by? It might be legally more satisfactory for both patient and doctor if at all stages of a disciplinary inquiry there were present persons trained to assess evidence, to ascertain facts, and to interpret law as laid down in Orders and Regulations. Above all, there should be strict impartiality. What stands out in the present picture is the overriding power of the Minister, and this means in effect the Ministry of Health. Their job surely is to administer; they cannot really be held to be either impartial or trained in deciding questions of fact or in seeing that justice is done according to the rule of law.

It is good that the G.M.S. Committee is to re-examine the whole question. And no doubt it will do this on the basis of principle rather than of expediency. Only when it has sifted out the arguments for and against the present system will it be able to make constructive proposals, the nature of which will be awaited with interest.

A WORLD PHARMACOPOEIA

The publication by the World Health Organization of Volume I of the *Pharmacopoea Internationalis* is an event of some medical and pharmaceutical importance, since it goes a long way towards the international unification of the nomenclature, composition, and standards of medicinal substances. Uniformity in pharmacopoeial standards and formulae was recognized as desirable as long ago as the middle of the nineteenth century, particularly on the Continent of Europe. The various national pharmacopoeias showed differences in the nomenclature and specifications of drugs reflecting the differences in national medical and pharmaceutical practice. To quote the preface of the new volume, "Such differences in national standards for widely used material constitute a source of danger to travellers, who may need to have the same prescription dispensed in different countries . . . also are a hindrance to the spread of medical and pharmaceutical knowledge and to international commerce." Some progress was made towards the unification of pharmacopoeias by the international agreements of 1906 and 1929. The present book results from the work of an Expert Committee set up by the League of Nations in 1937, which since the second world war ended has continued under the auspices of W.H.O. English and French editions are now ready, and a Spanish edition is expected shortly. The volume is similar in form to the present-day national pharmacopoeias. The official names of the drugs are in Latin. Drugs of long-established therapeutic interest which are common to a number of national pharmacopoeias are included, but the subject-matter is not restricted to these.

The book comprises some 200 monographs containing descriptions, standards, tests, and assays designed to provide as complete a specification as possible for each drug. There are 43 appendices defining general tests and methods and containing other data necessary for the understanding and use of the monographs. The methods described in the appendices have been made as complete and definite as possible so as to offer precise guidance to pharmacists and manufacturers in under-developed countries. Besides the vegetable, inorganic, and organic substances which are described in most pharmacopoeias, there are monographs on sera, vitamins, hormones, and a selection from the range of sulphonamides and barbiturates. The monographs, in fact, cover a representative selection of the most valuable members of the various pharmacological groups—including, among others, anaesthetics, analgesics, antimalarials, and hypnotics. The vegetable drugs of the *International Pharmacopoeia* are restricted to those which have definite therapeutic activity and can be assayed chemically or biologically (opium, digitalis, ergot, belladonna, ipecacuanha, etc.). Volume II, which is to be published in 1952, will include penicillin, streptomycin and other antibiotics, the various forms of insulin, solutions for injection, compressed tablets, certain tinctures, and some of the newer synthetic remedies.

FAILED B.M.

On Tuesday this week Convocation at Oxford decided that from now on the names of candidates for the degree of Bachelor of Medicine and Bachelor of Music are to be published. If this is done it will be possible for the curious—and curiosity is not always benevolent—to find out which candidates have failed when the pass list is finally published. When this question of publishing lists was recently debated in Congregation controversy was acute: 91 voted for and 61 against publishing the lists of candidates. As the necessary two-thirds majority was not obtained the matter was referred to Convocation. In Congregation Dr. A. G. Ogston, a Fellow of Balliol College, based his opposition on the argument that passing the examination for Bachelor of Medicine gave the candidate the legal right to practise. He believed that the publication of pre-examination lists might subsequently prejudice the position of a doctor if it remained possible for unqualified people to inspect his academic record. The medical faculty at Oxford is opposed to this measure, and the other University authorities wish to introduce it simply to bring it into line with the practice of publishing lists of candidates for other degrees. Dr. Ogston pointed out that the practice of disclosing details of previous failure was not favoured by the Medical Defence Union or by the medical authorities of Cambridge,

London, Edinburgh, Manchester, and Birmingham.[1] The Conjoint Board of the Royal Colleges regards the fact that the candidate has failed as confidential. Surely this is right. A doctor's licence to practise depends upon his having passed examinations which entitle his name to be entered in the *Medical Register*. Whether he gets there, so to speak, with one shot or several is entirely beside the point. Oxford may believe that open confession is good for the soul, but we trust it will think once more of the implications of compulsory confession of failure in an examination which gives the successful candidate a legal right to practise a profession.

DEFICIENCY DISEASES IN JAPANESE PRISON CAMPS

In a recent report to the Medical Research Council Smith and Woodruff give a full account of the effect of a poor Asiatic diet on a large group of European prisoners and internees.[2] It is based on their own observations and those of their colleagues during three and a half years as prisoners in Singapore, Hong Kong, and Shanghai. As befits an M.R.C. report, the objective attitude is impeccable, and it is difficult to realize that all the information that is so carefully recorded was obtained by persons who themselves were subject to this large-scale "experiment" and who must have suffered from some of the deficiencies they describe. There is no mention that the very paper on which these observations were first recorded was incredibly precious and that towards the end the Japanese made repeated attempts to obtain and destroy all damaging written evidence of this nature. The insolence and callousness of the Japanese towards the sick are unemotionally described. In 1945, for instance, it was estimated by the British and Australian medical officers that 87% of the camp population were unfit for work. The Japanese disregarded these findings and forced sick men to go on working: "sickness correspondingly increased and its punishment ensued, a starvation scale of rations for the victims."

Many of the deficiency syndromes described—such as beriberi, pellagra, and the orogenital syndrome of riboflavin deficiency—are already well known. The great interest of the report lies in the account given of those less familiar manifestations of deficiency which, in these camps, were seen by the hundred. There was a high incidence of neurological syndromes, including amblyopia, spastic paraplegia, burning feet, and Wernicke's disease. In many of these it was not possible to define which particular vitamin deficiency was causal, but the large number of cases enabled repeated therapeutic trials to be undertaken, and the results have considerably narrowed the field. Even when the particular vitamin deficiency was known, the authors pertinently ask the reason why, "of a group of apparently similar men, in similar circumstances, on diets similarly deficient of B_1, one should get neuritis, another oedema, a third should die of sudden heart failure, and a fourth be apparently perfectly well." The ceaseless search to obtain concentrated forms of naturally occurring vitamins makes fascinating reading. Shark's liver oil was used for vitamin A; a watery extract of rice polishings acidified with 10 drops of "battery sulphuric acid" gave a B_1 concentrate; and for the remainder of the B complex (more especially riboflavin) an extract of grass or green leaves was used. In one camp this was produced at the rate of 20,000 gallons a year, from 300 tons of grass. This preparation was found to be a most effective treatment for amblyopia, and the ingenuity and resourcefulness which stimulated this scale of production prevented many from becoming blind.

It is interesting to note that there was no relation between malnutrition and overcrowding on the one hand and the incidence of tuberculosis and mental disease on the other. Except in Japan, tuberculosis was rarely seen in prisoner-of-war camps in the Far East, and its occurrence is not even mentioned in this report. This is in contrast to the much higher incidence among British prisoners-of-war in Germany, despite better food and physical conditions. Mental disorders were rare: only seven admissions out of a total of 11,000 in one year to Changi hospital were classified as mental. When depression (not amounting to insanity) occurred, the authors point out that "it had a very destructive effect on physical well-being. In all camps the individuals who kept fittest were those who worked hard and kept themselves cheerful and occupied. This report is concerned with failures of physical adaptation, but it is also a tribute to the intellectual and emotional adaptability of those who combined in its preparation.

THE B.J.I.M.

The latest issue of the quarterly *British Journal of Industrial Medicine*[1] is one of the most imaginatively edited specialist periodicals to appear for some time. As an international number on industrial medicine there is something in it to interest not only the industrial medical officer but everybody practising in an industrial area—discussions of aspects of rope-making, boiler-scaling, the chromate industry, mining, and of poisoning by lead, mercury, trichlorethylene, D.N.O.C., and methylal, as well as a stimulating and interesting paper by Sir Frederic Bartlett on the study of human skills. The two opening papers—the first by Dr. A. Grut on the International Labour Organization and the second by Dr. Sven Forssman on W.H.O.'s work to improve occupational health—describe the good that comes from nations working together, and there is a useful account, aptly entitled "Entente Radiologique," by members of the Pneumoconiosis Research Unit of meetings held between French and British doctors with the object of obtaining agreements on the classification of radiographs in pneumoconiosis. Large photographic illustrations and really critical book reviews are further testimony to an editorial policy which has been carefully thought out and carried through the whole journal.

[1] *Manchester Guardian*, November 16, 1951.
[2] *Deficiency Diseases in Japanese Prison Camps, Spec. Rep. Ser. med. Res. Coun., Lond.*, 1951, H.M.S.O., London.

[1] International Number, October, 1951, 8, No. 4, price 7s. 6d.: yearly subscription 30s.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

COMMON SPINAL DEFORMITIES IN CHILDREN

BY

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Deformity of the spine in the growing child is common, yet it is unusual for this to become serious. The parents' anxiety, however, is often considerable, usually because they have no accurate idea of what may happen. Much has been written on the subject of spinal deformities, for it excited interest even before the beginnings of modern medicine. This has not, unfortunately, led to clarification; indeed, there can be few other medical topics with so much confusion of ideas, and with so many loose and contradictory statements, as occur in the writings on this subject. It is not too much to claim that recent knowledge has simplified the problem.

Our classification is simple: the deformity is either an alteration of the normal antero-posterior curves or the occurrence of lateral curvature. Both these groups may be subdivided into the postural and structural deformities. The postural may be voluntarily corrected by the patient—it is an abnormality of muscular control; the structural deformity cannot be so corrected, because there is an alteration of vertebral shape.

Postural abnormalities are common and relatively unimportant; they do *not* change into structural deformities. The belief that they can do so has led to much confusion and much unnecessary treatment and worry. This statement is so fundamental that it is worth expressing again in another way. Structural deformities are the only ones which can become serious; they are structural from their beginning, and are never capable of complete correction by voluntary effort.

The normal antero-posterior curves cannot be obliterated, because of the special shape of the vertebrae and disks in each region; but because these curves have mobility they are capable of voluntary alteration. In normal posture the curves are held by the reflex activity of the muscles maintaining the erect position, in which the head must be over the pelvis if we are to keep our balance. In addition to this position of the spine, the tilt of the pelvis is capable of alteration, and, since the pelvis forms the base of the column, alterations of pelvic inclination must alter the alignment of the spine. Whether it is primarily the alteration of pelvic inclination or of the spine, or both, which causes these deformities is unknown.

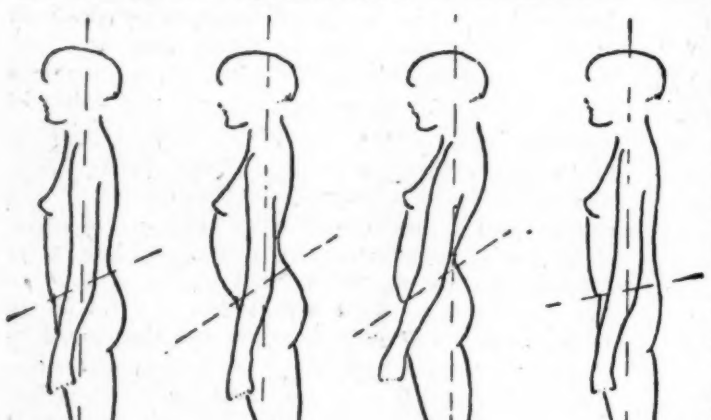

FIG. 1.—These figures, of which A is the normal, illustrate the various types of postural aberration of the antero-posterior curves. (Reproduced from *Essentials of Orthopaedics* by kind permission of Mr. Philip Wiles and Messrs. J. and A. Churchill, Ltd.)

I.—ANTERO-POSTERIOR CURVES

Clinically, we must first look at the lumbar curve to see if it is increased or reduced, then at the amount of thoracic kyphos—whether it is normal or increased. The diagnosis of this group as a whole is not difficult, as all abnormalities are correctable and structural change is thereby excluded. Infantile paralysis may easily mimic these conditions; for example, weakness of the abdominal muscles may give a lumbar lordosis and protuberant abdomen. Clinical testing of the muscles will, however, clearly show weakness if due to poliomyelitis. Limitation of movement and pain on movement implies some other change—for example, tuberculosis.

Wiles has described four types, each with its characteristic abnormality of spine and pelvis.

Lumbar Lordosis (Fig. 1 B).—Here the obvious abnormality is the prominent abdomen and hollow back or exaggerated lumbar lordosis. There may be a slight exaggeration of the dorsal kyphos, the shoulders may sag, and the head poke forward. It can be seen that the pelvis is inclined forward, and the spine may be said to be compensating for this by increasing the lumbar lordosis in order to maintain balance. There are, of course, no fixed deformities and the spine is fully mobile. The condition is completely corrected by contracting the glutei and the abdominal muscles.

Sway Back (Fig. 1 C).—This deformity is very similar in that there is a protuberant abdomen, sloping shoulders, and forward pelvic inclination. The lumbar spine, however, instead of compensating by increasing the general lordosis, seems to lean back acutely from the lumbo-sacral region. This is because of an additional deformity of increased thoracic kyphosis.

Round Back.—This deformity is the opposite of the last, in that the forward inclination of the pelvis is less than normal, lumbar lordosis is absent, and the "round back" is produced by an increased kyphosis of the thoracic or thoracolumbar spine. Frequently this condition presents as round shoulders, but round shoulders always mean that there is some abnormality of the spine.

Flat Back (Fig. 1 D).—The fourth type, as its name implies, is a lack of the normal curves. The pelvic inclination is reduced; as a compensatory phenomenon the lumbar lordosis is also reduced and the normal thoracic curve is absent, giving a flat back.

Treatment

Treatment is confined to exercises and the learning of a normal postural stance so that it becomes an unconscious habit. This is not easy to produce and takes time. The posture will improve in any case when an age is reached when personal appearance becomes important. It can be clearly stated, moreover, that these postural deformities do not lead to any other serious deformity. With this appreciated, excessive treatment, nagging of the child, and undue parental worry should be avoidable. These postural conditions may perhaps predispose to later backache but to nothing else.

Structural Kyphosis

A gradual development of kyphosis in an adolescent child is due either to tuberculosis or to epiphysial change; the former is generally angular and localized to a few vertebrae.

"Adolescent kyphosis," or Scheurmann's epiphysial osteochondritis of the spine, is a common condition starting about the age of 11 to 14. There is little or no pain, but the slow development of a thoracic or thoraco-lumbar kyphos is noted. This curve is long and not sharply angulated, and, being structural, is not completely correctable. Short hamstrings are often associated with it, possibly as a causative factor. The cause is an irregularity of the growth of the vertebral epiphysial plates, with consequent wedging and sometimes irregularity of the vertebral bodies. In the thoraco-lumbar region the epiphysial change may show on the skiagram as a deep notching of the anterior edge of the vertebrae rather than wedging. Lateral skiagrams rarely leave the diagnosis in doubt; in tuberculosis there will be bone and disk destruction, in Scheurmann's disease only the changes already described.

Scheurmann's disease is self-limiting, since at the end of growth no further change occurs. It has no serious consequence except for the deformity and a liability to slight pain in later life. Recumbency will prevent further increase of deformity, but there is some doubt whether this or a night plaster bed is actually corrective. Frequently it is discovered late, when growth has all but ceased, and then no treatment is of value.

II.—LATERAL CURVATURE

Postural Scoliosis

Children with postural scoliosis have a very slight single or total curve, more usually to the left. On bending forward, the curve disappears and it can be seen that there is no rotation of the vertebrae. This absolutely excludes structural scoliosis and is the most important diagnostic test. Compensatory scoliosis due to a short leg or deformed hip can mimic postural curvature, therefore the legs require to be examined and measured, and, if necessary, levelled by a block under the short leg.

If, then, a child has a single lateral curve without rotation, and with normal legs and normal hips, we should make a diagnosis of postural scoliosis. A skiagram of the spine taken supine will show no abnormality; taken erect it will show a single curve with almost no rotation, even radiologically, as shown by the spinous processes retaining their normal midline position.

Treatment is unnecessary, as the condition rights itself. although remedial exercises to improve the general posture are sometimes advised. This curvature has no clinical importance. We now know that postural scoliosis is *not* a precursor of structural scoliosis; the one never changes into the other.

Structural Scoliosis

In postural scoliosis there is never fixed rotation; structural scoliosis is never seen without it, however slight may be the lateral curvature (Fig. 2). In addition

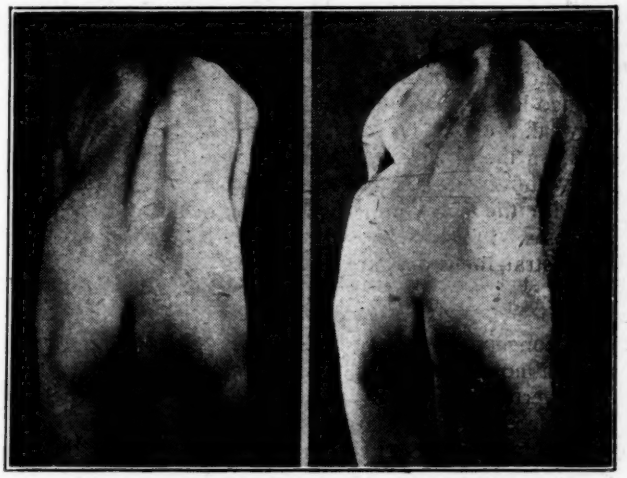

FIG. 2.—Photographs of a girl with a right thoracic structural scoliosis taken at a year's interval. The left-hand one shows a slight curvature to the right with slight but quite definite rotation of the ribs on the same side. A year later both the curvature and the rotation had become more obvious. Note that in neither compensatory curves is there any fixed rotation on bending forward.

to this, we later see secondary lateral wedging of the vertebral bodies and rotation and bony deformity of the thoracic rib cage.

In scoliosis there are usually three curves, the middle one of which is primary. Rarely there are two, the lower being primary, and it then will start at lumbar 5, leaving no room for the lower compensatory curve. Usually such a curve is congenital. In idiopathic scoliosis we may see four curves, in which case the middle two will be primary. The primary or major curve is characteristically rigid, and with marked fixed rotation and wedging. Clinically it will show the most rotation, and frequently it is the only one of the curves showing fixed rotation as demonstrated when the child bends forward. In adult life the rotation of the compensatory curve, which is always visible on the skiagram, becomes so fixed that it may also be present on forward bending.

Except in paralytic scoliosis, increase in curvature ceases at the end of growth. The age when this happens is very variable, from 11 to 18 years, and is dependent on the speed of skeletal maturation. In most girls the onset of menstruation, and in both sexes the complete development of the iliac apophyses, give us a very reliable "end-point" to the disease. This recent observation is of great practical value

The causes of structural scoliosis are many, but the three most important are infantile paralysis, congenita.

bony abnormalities of the spine, and idiopathic curvature, the last being the commonest of all. If we confine ourselves to discussing these three types it must not be forgotten that many other conditions, such as neurofibromatosis, various neurological conditions, etc., may cause scoliosis, on occasions most severe.

Paralytic Scoliosis

Spinal deformity following paralysis of the trunk muscles due to poliomyelitis is like deformity occurring elsewhere in this disease, for it is related to the imbalance of muscle power. If we have a strong calf muscle and weak foot extensors, there will develop a severe and fixed drop-foot. With inequality of pull of the trunk muscles we shall get a fixed spinal curvature, whereas with total trunk muscle paralysis we may get little. Weakness of the intercostals on one side produces a thoracic curve; unilateral weakness of the lateral abdominal muscles will probably result in a severe thoraco-lumbar curve with its convexity on the side of the weak muscles. A total or equal paralysis on the two sides, on the other hand, gives rise to an unstable spine but without much fixed deformity, as in a flail limb. As with the flail limb, so with the unstable spine: it collapses, giving a severe curve when the patient is erect, but it straightens out on lying down.

Congenital Scoliosis

In congenital scoliosis it is the angulation caused by bony abnormalities which causes a curvature. A single hemi-vertebra may tilt the spine seriously, whereas multiple and bizarre congenital spinal abnormalities may give numerous small and opposite curves, the overall effect of which may be to give a clinically straight spine. It is difficult, however, to prognosticate on any case at an early age.

Idiopathic Scoliosis

The cause of this condition remains a mystery. There is not even an attractive hypothesis. A once widely held belief that it was the result of unrecognized poliomyelitis does nothing to explain its great predominance in girls, or that biopsy of muscle shows no abnormality and that the characteristic patterns of idiopathic and paralytic curvature are easily distinguishable.

Though its cause is unknown its natural history is becoming understood, and we now know enough of the way this disease behaves to give a reasonably accurate prognosis for any individual patient. The site and extent of the primary curve can be related to the natural evolution of the disease. There are several curve patterns, each with its definite and characteristic prognosis. This is the most important recent advance, and it is of great practical value, for only 5–10% of idiopathic structural curves are important. We are now able to predict which type of curve may become severe.

Another important prognostic factor is the age of onset. Idiopathic scoliosis starts at any age from a few months to 15 years, most commonly between 10 and 12 years of age, but the earlier it starts the worse it may become. Despite this, however, many curves of early onset do not become severe, for scoliosis often ceases to progress without treatment and during active growth.

We may now briefly review the natural history of this disease. In its idiopathic form the position of the primary curve is the key to the prognosis, and the following is a brief outline of the four main patterns.

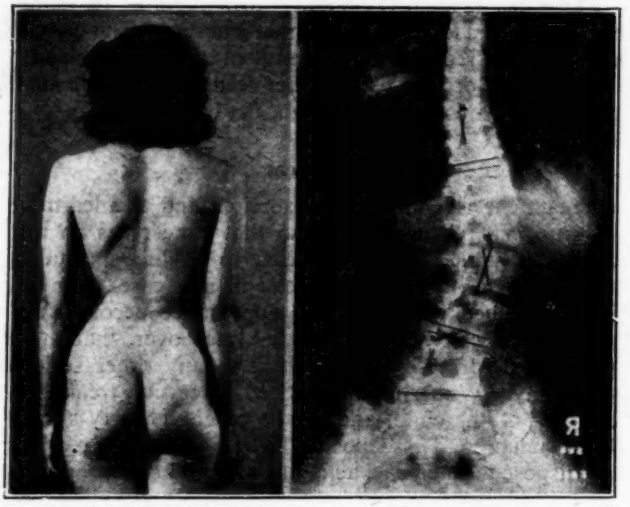

FIG. 3.—Lumbar idiopathic scoliosis. A fairly typical example of benign idiopathic scoliosis. The apex of this curve is at lumbar 1 and there are compensatory curves above and below. Note that the apophyses have grown round to the posterior superior spines. Growth has ceased and this curve will not now increase. (Reproduced from the *Journal of Bone and Joint Surgery*, by kind permission.)

Primary Lumbar (Fig. 3).—The primary curve is lumbar with the apex at lumbar 1–2 or 3. It often starts in adolescence and is never severe. We can always say that this type of curvature will cause so little deformity that it will not be easily detected in the clothed patient. It never requires correction and fusion. It often causes backache in later life, however, owing to osteoarthritic degeneration of the posterior joints.

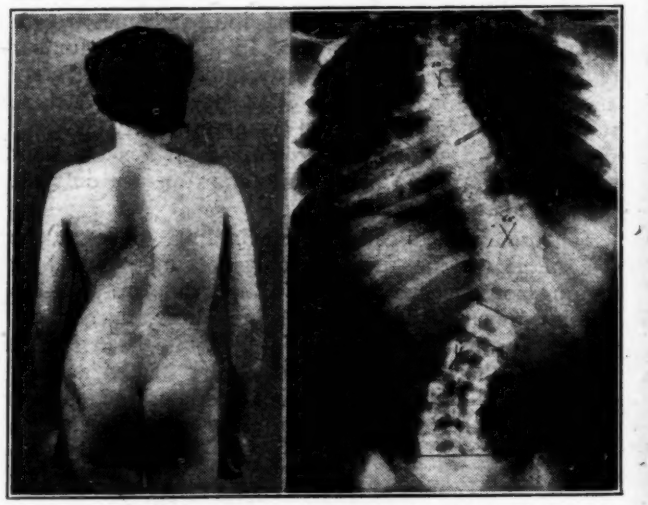

FIG. 4.—Thoraco-lumbar idiopathic scoliosis. A curvature intermediate between that of the lumbar and thoracic patterns. It usually has a good prognosis, and this may be regarded as a fairly average final deformity. Note the rotation; the apophyses can be seen to have completed their growth.

Primary Thoraco-lumbar (Fig. 4).—Here the apex is a little higher, usually at thoracic 11 or 12. Whilst behaving mildly in nearly all cases, like the lumbar, it occasionally behaves more like thoracic scoliosis and requires correction and fusion.

Primary Thoracic (Fig. 5).—This is the most important pattern, since all severely deforming idiopathic scolioses come from this group. It most often starts soon after 10 years of age, usually in girls and almost always to the right; the apex will be mid-thoracic. Progress is sometimes rapid, and, because of the severe curvature and

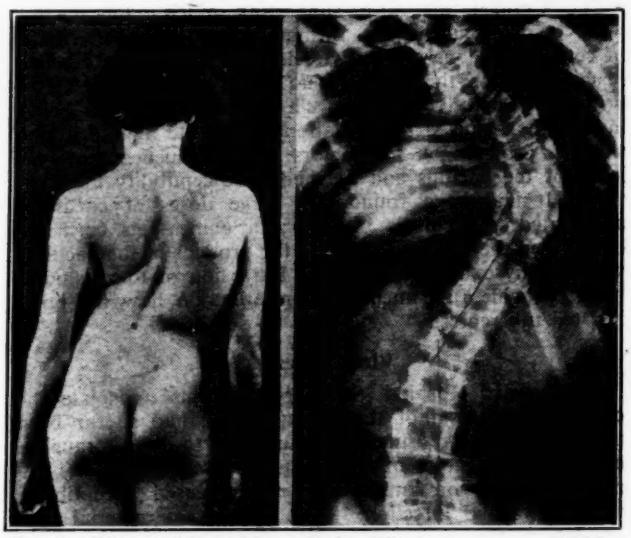

FIG. 5.—Thoracic idiopathic scoliosis. This is the pattern with the bad prognosis. Note the marked rotation of the ribs, the low left shoulder; and the prominent left hip (obscured by the arm). This girl has since been corrected and her vertebrae have been fused because of her present deformity and bad prognosis.

because the ribs are involved in the rotation, deformity is great. Despite its bad prognosis, in only a minority even of this pattern does it become ugly enough to require correction.

There is a small separate group within this curve pattern. It is an idiopathic thoracic scoliosis starting in infants, usually in boys, and nearly always with a left

FIG. 6.—Combined thoracic and lumbar idiopathic scoliosis. There are four curves and the two primary are keeping in step, the thoracic being 68 degrees and the lumbar 66 degrees. There is a double rotation, but the shoulders are level and the hips covered. The skiagram looks bad, but the cosmetic appearance is good.

curve. Because it is a thoracic primary curve and has so many years in which to deteriorate, it has a serious prognosis.

Combined Thoracic and Lumbar (Fig. 6).—This pattern with four curves has the two primaries in the middle and in opposite directions. This quadruple pattern in which the primary lumbar and thoracic curves usually maintain the same degree of curvature has a reasonably good prognosis. The *x*-ray appearance may be formidable, but the child's appearance is good because the opposite rotations balance one another; the shoulders remain level and the hips do not stick out. Clothes hang well. Correction is therefore almost never indicated; it would indeed be a formidable procedure, as here one would have to correct curves in opposite directions and graft two primary curves.

Treatment

When Ferguson and Cobb devised accurate methods of measuring curves the effect of treatment could be estimated objectively, the assessment no longer depending on the often too optimistic visual impression. It was shown that conservative treatment by exercises, plasters, spinal supports, etc., never improved a structural scoliosis. It is true that the child might learn to stand better and look a little better, but the degree of curvature never improved. Recumbency during growth, a usually impracticable method, is the only way in which a progressing curve can be arrested. It is now becoming doubtful whether other conservative methods can ever do this.

At first this denial of the value of conservative treatment makes depressing reading. Against this we must set the immense value of being able to say which cases of scoliosis may be severe. Previously, when no distinction between one type of curve and another could be made, any one of a hundred cases might become severe; now we can immediately exclude at least 75% of them. It means that long hours away from school (at school certificate age) to attend hospital for exercises, the wearing of supports, and the restriction of activities can be avoided in those cases in which it is certain the prognosis is good.

It is essential to watch these children grow up, and to take skiagrams at intervals of several months, in order to measure and record the degree of curvature. During growth 5–10% of the children will develop a severe deformity. This small group must be carefully followed and, if indicated by the amount of deformity present or expected, correction and fusion advised. What is more, we may correct and fuse before the deformity is severe, when treatment will be both easy and rewarding. For the remaining cases no treatment is indicated. With modifications, this regime is applicable to all types of scoliosis, irrespective of aetiology. However, paralytic scoliosis requires correction and fusion more often than the idiopathic type.

While this is not the place to discuss in detail the surgical treatment of scoliosis, it will be useful to indicate what may be expected of operation. The generally accepted method is to correct a curve by a plaster turnbuckle jacket as devised by Risser. When corrected to the amount possible (over-correction is a greater danger than under-correction), the spine is fused over the extent of the primary curve. Then the child is kept recumbent and held corrected for six months while the graft fuses. Subsequently a plastic support is used for a further six months, after which it can usually be discarded. The result one can expect is that the shoulders will be level, and the prominent hip covered, but the backward rotation of the ribs on the convexity of a thoracic curve will be only partially corrected. The general effect is to increase the height and permit the wearing of normal clothes without visible deformity, a matter of great importance in a disease which is so largely an affliction of otherwise healthy adolescent girls. The additional rigidity of the spine caused by the fusion itself is usually negligible, since it is usually a thoracic

fusion and a primary scoliotic curve is already almost immobile.

While this procedure is tedious and time-consuming, it is not unduly hazardous, particularly now that frozen banked bone is used for the graft. Experimental work is being done with the object of arresting the growth of the epiphyses on the convexity. If this can be made a practical procedure it will considerably simplify the operative treatment of scoliosis.

PROGRESS IN MEDICAL RESEARCH 1948 TO 1950

The following account is a much condensed version of the chapter in the Medical Research Council's recently issued Report to Parliament, headed "Some Aspects of Medical Research in the Period 1948–1950."*

Chemotherapy and Antibiotics

One of the principal reasons for the transfer of the National Institute for Medical Research from its old quarters in Hampstead to the much larger building at Mill Hill had been the need for expansion of research in chemotherapy. Particular attention had been given in the Council's laboratories to the chemotherapy of tropical disease. In amoebic dysentery several new compounds had been discovered which were almost as active as emetine and considerably less toxic. The most promising of these drugs would shortly be submitted to clinical trial. The Council's Bilharzia Research Group, working in Egypt, had tested the German drug "miracil," which had been found capable of curing about 30% of those with schistosomiasis. In the treatment of filariasis "hetrazan" had been studied; it had been shown to clear the peripheral blood of filarial larvae by making them susceptible to attack by leucocytes. Experimental studies had established that the lungs formed a reservoir for the larvae, from which they emerged at night into the blood stream.

To have a rational basis for the development of chemotherapeutic research it was necessary to understand the mode of action of a drug on the micro-organism under attack. The Council had therefore given much attention to the study of the biochemistry of micro-organisms. Work at Cambridge had now shown that one action of penicillin on bacteria was to prevent their assimilating a certain amino-acid which they needed. Similarly the widely pursued investigations of bacterial enzymes and growth factors might at any time disclose biological properties of bacteria which would cast light on their susceptibility to drugs.

Tuberculosis

The major chemotherapeutic advance in this field had been the discovery that the development of resistance to streptomycin could be minimized if *p*-aminosalicylic acid (P.A.S.) was given at the same time. The work of the Council's Tuberculosis Research Unit had contributed to this advance: the precision with which it had been possible to define the value and limitations of these drugs had been due in no small measure to its rigorously controlled clinical trials. In the field of prevention, the same unit was carrying out an investigation into the effect of B.C.G. vaccine on children about to leave school, a particularly vulnerable group so far as tuberculosis was concerned. A vaccine containing a strain of tubercle bacillus discovered in voles was also being tested; this vaccine was probably more stable than B.C.G.

The Council was also supporting much experimental work on tuberculosis. In Birmingham the harmful effects of certain fractions of the tubercle bacillus, and the defence reactions which they elicit, were being studied. At Cambridge the reproductive life-cycle of the bacillus was being investigated, and at the National Institute investigations were in progress on the factors which influence the virulence of the bacillus and the body's susceptibility to infection. It had been found that large doses of cortisone aggravated tuberculosis in mice; in guinea-pigs cortisone diminished the tissue response to the proteins of the bacillus, whereas thyroxine increased it. Extension of those studies might provide fundamental information on how the body resisted tuberculosis.

Virus Diseases

At Harvard Hospital, Salisbury, attempts to isolate the causative organism of the common cold had so far been unsuccessful. Exposure of volunteers to cold draughts, exercise to the point of fatigue in rain, wet socks, etc., had neither brought on natural colds nor increased susceptibility to experimental infection. With fluorescent material as a marker, it had been shown that the transfer of infective secretions was very much greater by direct contact than through the air, but an attempt to reduce the spread of respiratory infection by the use of self-sterilizing, impregnated handkerchiefs had not succeeded.

A small-scale study at Harvard Hospital had shown that antihistamine drugs had no prophylactic effect against artificially induced colds. In addition, a large-scale and carefully controlled clinical trial of the effects of another antihistamine drug against naturally occurring colds had shown that the drug had little or no value. A second large-scale trial had given similar results.

After the establishment of the World Influenza Centre at the National Institute it had proved possible to trace the 1948–9 influenza epidemic from Northern Sardinia right across Northern Europe to Great Britain, Denmark, and Iceland, and to prove that a true country-to-country spread had occurred. During that epidemic Dr. W. J. Elford and his colleagues at the National Institute had made an unexpected discovery. Using a new technique, Dr. Elford saw under the electron microscope pictures of pigment-free "ghosts" of red cells with small round virus bodies all over them. Freshly isolated influenza viruses obtained in 1949 were unexpectedly found to exist largely in the form of long filaments having about the same diameter as the small round bodies previously observed; some of the pictures apparently showed the presence of round forms within the long filaments. After being cultivated in the laboratory for some time, the viruses tended to revert to the "classical" spherical form. This work, together with other similar work on the virus of fowl plague, provided entirely new ideas about the possible life-cycles or modes of multiplication in this group of viruses. In this connexion, Dr. L. Hoyle, at Northampton, had suggested that after injection into the fertile egg influenza virus might break up into fine particles which reproduce themselves before coming together in some way to reconstitute the normal virus bodies.

Work on poliomyelitis had been directed to surveying the distribution of the virus throughout England and Wales during epidemic and inter-epidemic periods, and to an epidemiological inquiry into the part played by various factors, in particular protective inoculations, in the activation of latent infections. An analysis at the Council's Statistical Research Unit had led to the conclusion that inoculation within the month preceding the onset of illness had in some cases caused the paralysis to be localized in the injected limb. This subject was being further investigated.

Q Fever

The rickettsial disease Q fever was first described in Australia in 1937, transmission being from infected cattle. Since then the disease had been reported from Italy, parts of the United States, Central America, Switzerland, Germany,

*Report of the Medical Research Council for the Years 1948–1950. (1951.) Cmd. 8387. H.M.S.O.

Turkey, and Israel. In 1949 the first cases of Q fever in Britain were recognized clinically, and *Rickettsia burneti* was recovered from them at the Virus Reference Laboratory of the Public Health Laboratory Service. The two cases were in a pathologist and nurse who had had contact with a patient from Kent dying of a pulmonary infection later shown to be Q fever. Further investigation showed that his wife was also infected, and *R. burneti* was finally isolated from the milk coming from two local herds from which this family had been supplied. Investigations were now in progress to delineate the extent of the infection among livestock in Britain.

Cortisone and A.C.T.H.

Although only small amounts of either substance had been available, the Council had already embarked on a substantial programme of clinical and experimental research. Hitherto cortisone had been manufactured by an elaborate and expensive synthesis starting from deoxycholic acid, a steroid in ox bile. Such raw material must always be scarce. Efforts were therefore being made to replace it with a steroid of vegetable origin, and the Council had sent an expedition to Nigeria, where likely plants were thought to exist. Attempts were also being made to find some cheaper substance that would reproduce its action.

Home production of A.C.T.H. had been encouraged, but there were still many difficulties to overcome. If, as had been suggested by Dr. C. J. O. R. Morris and Dr. Li in America, the activity of A.C.T.H. was due to a fraction of the whole molecule, its synthesis might eventually be possible.

Methonium Compounds

As a sequel to the isolation of D-tubocurarine by Dr. Harold King, attempts were made to replace the curare alkaloids by synthetic substances. In the course of this work the group of drugs known as the methonium compounds had been synthesized and studied by Dr. King, Dr. W. D. M. Paton, and Dr. W. J. Zaimis. These were shown to have a mode of action quite different from curare. The ten-carbon member of this series, C10, had proved outstandingly active and was given clinical trial in anaesthesia and for the modification of electric convulsion treatment. Clinically, what might be the most important application of the methonium drugs had been developed from the observation that the shorter-chain members of the series could paralyse the autonomic nervous system, hexamethonium in particular having a powerful action on the ganglia. That work had already been followed up clinically in the treatment of hypertension and peptic ulcer.

Biological Standardization

The Department of Biological Standards at the National Institute had continued to act as a world centre for the distribution of 21 international standards. New standards had been made for streptomycin, provitamin A, A.C.T.H., and (with the Lister Institute) anti-A and anti-B blood-grouping sera. The requirements of this country for the control of certain drugs had been met by establishing provisional British standards for globin zinc insulin, dihydrostreptomycin, D-tubocurarine, dimercaprol, hyaluronidase, and oxophenarsine. As a result of work by Dr. A. A. Miles, biological assays depending on skin reactions had been made more precise.

Biochemical Research

At the earliest possible date the Council had obtained supplies of radioactive isotopes from the United States and arranged for their distribution to research workers. In addition, work had been carried out on the design of radioactive assay apparatus. The most extensive use of isotopes at the National Institute had been in studying the way in which biologically important compounds are formed in the body. Work on haemoglobin had now made it possible to suggest a complete chemical mechanism for the formation of porphyrin. This work had been extended to studies of erythropoiesis and acute porphyria. Fat metabolism in the foetus had also been studied; as a result it had been concluded that carbohydrate must be the main source of energy for the growing embryo. Another problem had been the process by which milk fat was built up.

Attempts had been made to explain the specific biological activity of proteins in terms of their chemical structure. Physico-chemical researches had been directed to the separation of proteins in the pure state. In collaboration with Sir Edward Mellanby the toxic agent responsible for fits in dogs fed on agenized flour had been identified as methionine sulphoximine. A mixture of peptides derived from *Bacillus licheniformis* and called licheniformin had been shown to be active against the tubercle bacillus; unfortunately, it had been too toxic for clinical use. At Sheffield work was in progress on the maintenance of the normal potassium content of the cells, disturbance of which was so notable after surgical operations and in shock, and on the mechanism of secretion of acid in the stomach.

Biological Aspects of Atomic Physics

The effects of radiation on individual cells and tissues had been studied both experimentally and clinically. Work had also been done to discover what factors might diminish the response of the animal body to ionizing radiation. Two sulphur-containing organic compounds had been shown to have some protective effect when given before radiation.

Tracer elements had been used to study biochemical processes—for example, radio-phosphorus for the rapid estimation of the blood volume, radioactive iodine to measure thyroid function, and radio-sodium to indicate when the new blood supply in a pedicle skin graft was vigorous enough for the graft to be safely transferred. At Hammersmith Hospital the construction of a cyclotron and linear accelerator had made good progress. Cases of cancer of the lung treated by medium *x*-ray therapy and surgery were now being collected for later comparison with those given supervoltage therapy. Radioactive iodine and radio-phosphorus had been used respectively for certain cases of thyroid cancer and disease of the bone marrow. Colloidal radio-gold had been used for the treatment of generalized cancer of the body cavities, and radio-cobalt and other isotopes were being investigated as convenient substitutes for radium.

Cancer Research

The search for substances to attack the cancerous cell continued. So far the only types of malignant growth to show a significant response were those affecting the blood cells, the lymphatic tissues, and the prostate gland. The role of cutting oils in the production of skin cancer in the engineering industry was being examined, and also the relationship of tobacco smoking to cancer of the lung. A carefully controlled survey had indicated that the incidence of lung cancer was related to the habit of tobacco smoking. Sir Ernest Kennaway had studied the possible effects of arsenic (found in some brands of tobacco), and of benzpyrene and radon from the atmosphere, in causing lung cancer.

Blood Groups and Blood Transfusion

In genetics, blood groups had rapidly assumed a key position because more was known about their inheritance than about any other human characteristic, and because of the close chemical similarity of the blood-group substances to the genes which determine them. In 1949 Dr. R. R. Race had announced that almost a million genetically different combinations of blood-group factors were known. Dr. A. E. Mourant had applied blood-grouping to the study of racial differences and for tracing the origins of populations. Dr. P. L. Mollison and his colleagues had recently brought to light the previously unrecognized "Duffy" system of blood groups, and had devised objective methods for measuring

the severity of haemolytic disease of the newborn The Council's Blood Products Research Unit was drying the plasma from over 2,000 blood donations each week. A useful development had been the splitting up of plasma into fractions, such as gamma globulin, fibrinogen, and thrombin. Trials had been carried out with the carbohydrate substitute for plasma, "dextran"; and a non-toxic derivative had been produced which could be used to control the rate of blood clotting.

Studies in Undernutrition

One of the Council's units, under the direction of Professor R. A. McCance, had been stationed at Wuppertal, in Germany, from July, 1946, to January, 1949. A thorough investigation had been made of hunger oedema. In that condition the space previously occupied by solid organs before their diminution in size became filled by a fluid which resembled normal interstitial or lymphatic fluid. Antibody production was shown to be only slightly less efficient in the undernourished than in normal people. The serum cholinesterase was found to be a useful index of nutrition. "Effort syndrome" appeared common among the undernourished and was responsible for many of the signs and symptoms commonly attributed to the physical effects of undernutrition.

Tropical Medicine

Many new drugs had been screened and their value and mode of action investigated. That work had been extended by clinical trials in suitable tropical areas. A Field Research Station had been established in the Gambia as part of the Human Nutrition Research Unit in London. There, under Professor B. S. Platt's direction, clinical and laboratory investigations had been carried out on the prominent problems of nutrition in the area, such as the role of parasitic disease in accelerating the consequences of malnutrition, the chemistry of tropical cereals and their processing, and the effect of deficiencies of tracer elements in the soil on plant growth. A field working party had also undertaken agricultural work to estimate the practicability and value of introducing modern methods of farming in a selected area.

Occupational Health

At Birmingham studies of minor injuries and skin diseases, two important causes of lost time, had been continued. Elsewhere much attention had been devoted to the problems created recently by the use of toxic weed-killers and insecticides in agriculture. As a result of work at Cardiff, pneumoconiosis had now been classified into two stages, the later stage ("progressive massive fibrosis") being thought to be due to a tuberculous process in a lung already damaged by "simple pneumoconiosis." To test this theory, an attempt was being made to diminish the risk of tuberculosis in a selected population, and to observe whether progressive massive fibrosis continued to develop among miners with simple pneumoconiosis.

A large-scale survey of the Disabled Persons Register had been carried out in Glasgow, Manchester, Birmingham, and London, and a series of special studies of notoriously incapacitating diseases had also been made. At Cambridge the factors which affect human skill, from simple manual dexterity to the exercise of rapid discrimination in complex intellectual situations, were being studied. Attention was also being given to the design of machines and machine tools. At the Maudsley Hospital an investigation into the possibilities of employing mental defectives was in progress.

Work on the clinical and physiological aspects of climatology had been greatly extended both at the new Division of Human Physiology at the National Institute, at special units in London and at Oxford, and at the Royal Naval Tropical Research Unit at Singapore. Work for the Services was also continuing in many of the Council's units, with a view to improving the health, comfort, safety, and efficiency of the country's defence forces.

Reports of Societies

CORTISONE AND THE EYE

A meeting of the Section of Ophthalmology of the Royal Society of Medicine was held on November 8 at 1, Wimpole Street, W.C.1, to discuss the action of cortisone in the tissue reactions of inflammation and repair, with special reference to the eye. The president, Professor W. J. B. RIDDELL, opened the discussion by saying that the discovery of cortisone and similar steroids was of fundamental importance in medicine, ranking with the discoveries of insulin, the sulphonamides, and penicillin.

Place in Clinical Ophthalmology

Sir STEWART DUKE-ELDER, discussing the application of cortisone in clinical ophthalmology, made it clear that little was yet known of how cortisone worked, or in what form this relatively insoluble substance entered the eye or tissue cells. It had a potent action in blocking acute inflammatory processes by reducing cellular exudate, decreasing abnormal capillary permeability, inhibiting the formation of new vessels and granulation tissue, and damping down the fibroblastic reaction of repair, no matter by what noxious stimulus the inflammation was produced. It did not, however, influence the underlying disease process, which would resume its characteristic course when the hormone was withdrawn. Hench described it as acting as a fireguard though it would not put out the fire. The congestive and exudative manifestations of acute inflammation, such as acute iridocyclitis, usually disappeared rapidly, and could be held in abeyance while cortisone was given. In chronic inflammation, although active exudative manifestations were often controlled, the inflammatory process tended to persist even during treatment, and on cessation the eye often resumed its former state or suffered early relapse.

In a delicate structure such as the eye, in which sight depends on optical transparency, the inhibition of a massive inflammatory reaction might allow its survival as a functioning organ. It was not, however, clear whether the apparently beneficial effects of cortisone were entirely without harm. The inflammatory reaction was thought to be defensive in purpose, and, while that reaction might sometimes be excessive, it was not yet certain whether complete passivity of the tissues could be produced with impunity, particularly in organismal infections.

Clinically it was especially sound practice to use cortisone to inhibit inflammation in the eye while the cause was being eliminated by other means, as in gonococcal iridocyclitis, or in self-limiting diseases such as interstitial keratitis. In tuberculosis, Sir Stewart said, the position was far from clear. He described two illustrative cases which suggested that, though cortisone might be valuable to control allergic manifestations, it might allow dangerous dissemination where infection was present. Surgery could, if necessary, be performed while inflammation was controlled by cortisone, for, although fibroblastic repair was inhibited, with the therapeutic doses used locally wound healing was adequate. There was evidence that the inhibition of new vessel formation and corneal opacity might be useful to maintain the clarity of corneal grafts.

Inhibition of Healing

Dr. NORMAN ASHTON discussed the action of cortisone on ocular inflammation and repair. A. Biegal had shown that intramuscular cortisone would inhibit the intraocular inflammatory reaction of horse-serum uveitis in rabbits. Dr. Ashton described experiments to show the effect of subconjunctival cortisone on the healing of perforating wounds of the rabbit cornea. Inhibition of the formation of fibrinous

coagulum, of cellular infiltration, endothelial regeneration, and fibroblastic repair, was evident in the treated eyes. The degree of inhibition of healing was related to the dosage of cortisone, being moderate with small doses when the final stage of healing was impaired but adequate, and severe with larger doses.

The inhibition of the growth of fibroblasts raised the question whether cortisone had a direct action on these cells. The work of A. S. Steen, using tissue cultures, had shown that this was not the case, as fibroblasts and epithelial cells grew normally in concentrations of cortisone much greater than the therapeutic levels. It was now generally believed that, in the defensive reaction of inflammation and in the reconstructive phase of proliferation, the noxious irritant, whatever its nature, played a smaller part than the products of the injured tissues themselves. These products had been shown to cause increase in capillary permeability and diapedesis of leucocytes, and might be responsible for the cell division which led to repair. Dr. Ashton said that, though our knowledge was very meagre, a study of the effects of cortisone on the release or action of these substances might be a fruitful field of inquiry.

Effect on the Capillaries

Mr. CHARLES COOK described experimental work on the influence of cortisone on capillary permeability and new vessel formation carried out in conjunction with Dr. Ashton and Dr. McDonald. Using the Amsler-Huber method of measuring capillary permeability to fluorescein, he had found that in man cortisone did not alter capillary permeability across the blood-aqueous barrier in the normal eye, but reduced the increased permeability which occurs in the inflamed eye. He had also carried out experiments using Langham's method of producing a minimal but standardized vascularizing lesion of the rabbit cornea by the injection of alloxan into the anterior chamber. Cortisone caused a reduction in the amount of new vessel formation, subconjunctival injection being more effective than intramuscular. Corneal opacity was partially, but not completely, inhibited by subconjunctival but not by systemic administration. He had as yet no definite evidence on whether the vascular inhibition was due to a direct effect of cortisone on the vascular endothelium, resembling the inhibition of corneal endothelial repair demonstrated in Dr. Ashton's experiments, or due to the blocking of response to chemotactic products of the inflamed tissue cells.

Discussion

Among those who took part in the discussion, Mr. D. P. GREAVES described experiments carried out with Mr. A. Lister, using thermal burns of the rabbit cornea. Their results had shown that cortisone exerted some inhibitory effect on the formation of new vessels whether administered systemically or locally, but the effect was more pronounced with local applications. Mr. B. W. RYCROFT described favourable experiences with the local use of cortisone on neo-vascularization after corneal grafting. Sir STEWART DUKE-ELDER considered that for inflammation of the anterior ocular segment local treatment was best, preferably by subconjunctival injections for inflammation of the inner eye. Instillation was usually satisfactory for corneal and conjunctival lesions. For inflammation of the posterior segment systemic treatment was best.

Local authorities should consider encouraging food traders to display a notice requesting customers, in the interests of hygiene, not to bring dogs into food shops and restaurants, says a circular which has just been issued by the Department of Health for Scotland. The circular states that the matter cannot be dealt with by regulation or other enactment, but the display of a notice signed by the medical officer of health might do good.

Correspondence

Bornholm Disease

SIR,—From time to time an epidemic of Bornholm disease, under this or one of its other titles, is recorded in the medical journals. The article is often followed by letters from other doctors, who recognize that they have unknowingly been dealing with similar cases. In spite of the efforts of Dr. W. M. Pickles for nearly twenty years to publicize its symptoms, and the ease with which an epidemic, though not individual cases, can be diagnosed, most epidemics still remain unidentified. May I refer to one?

In the latter months of 1941 and the early months of 1942 there was an extensive epidemic in the Army. I saw 80 to 100 cases in military hospitals in various parts of England. They were typical cases, and could have been diagnosed by anybody with a scant knowledge of the symptoms, but in not one single instance had the diagnosis been made. Many medical officers were even unaware of the existence of the disease. I called attention to the epidemic in a letter to the *British Medical Journal* (1942, 1, 736), but nobody took any notice.

The patients whom I saw had generally been admitted to the medical ward on account of the presence of a rub, and would certainly represent only a small fraction of those affected. For Bornholm disease, like other diseases, can occur in all degrees of severity, and does not by any means always conform to the picture of acute sudden onset of pain of great severity, which we derive from most clinical descriptions. Roche, who treated an epidemic among young soldiers in a military camp, records that the men were not ill, and, when asked if they would have continued at work in civilian life, the majority answered yes. In the absence of a rub, a diagnosis of muscular strain or fibrositis is often made.

I should like to refer to the origin of this rub. It is agreed that there is no cough and no pulmonary change in Bornholm disease. The pain is caused by movement and is not closely related to the rub when this is present. The rub may persist after the pain has subsided, or develop on the opposite side without any pain. It may be extremely loud and coarse and of a character which I have never heard in pleurisy, although in other instances it may be indistinguishable. I agree with Sylvest that it is not a pleural rub, but is of muscular origin, possibly from the sheath or tendon. Its incidence varies widely in different epidemics, but I have met with it in other epidemics than the one here referred to.

The infection and pain are probably centred in the diaphragm, and extend to muscles above and below the costal margin. The affected muscles may be tender, and on a few occasions I have seen definite swelling.

Non-fatal epidemic diseases which have no dramatic sequelae have great difficulty in obtaining recognition. Both glandular fever (infective mononucleosis) and Bornholm disease receive little attention in medical education, and still are frequently overlooked. But, although they are non-fatal, an erroneous diagnosis of a more serious disease may result in operation or other unnecessary treatment. The researches on Coxsackie viruses and the discovery that the viruses of both these diseases may affect the central nervous system, not only as a benign meningitis but also as encephalitis, may result in wider publicity.—I am, etc.,

London, W.1. HENRY TIDY.

"Primary Atypical Pneumonia"

SIR,—I was very interested in Squadron-Leader Philip W. Robertson and Dr. K. D. Forgan Morle's explanation (October 27, p. 994) of the primary atypical pneumonia syndrome. The theory of the pathology seems eminently reasonable. The authors, however, infer that the syndrome is an aspiration pneumonia which may be superimposed

upon any upper respiratory infection provided the necessary physical activity is maintained.

Upper respiratory catarrh is extremely common in this country, yet the syndrome of primary atypical pneumonia remains in general rare. When it does occur, in my experience it tends to be epidemic and characteristically is *not* preceded by upper respiratory infection. To me it is quite as clear an entity as measles or chicken-pox, and in these the organism or virus has not yet been isolated. It is almost invariably ushered in with an intense headache and with an oppressive pain behind the upper sternum. Neither of these symptoms was mentioned by Drs. Robertson and Morte.

The incubation period in the epidemics I have seen has been 12-18 days—i.e., the cases occurred in groups at this interval. Most occurred in schools. Response to "aureomycin" and "chloromycetin" has been dramatic; penicillin and sulphonamides have shown no therapeutic effect.

If we are to accept the authors' suggestion that the syndrome is due to the aspiration of catarrhal secretion it is curious that although the organisms of such secretions are almost all penicillin-sensitive, yet penicillin fails to lower the temperature or influence the condition, whereas aureomycin does. While perfectly prepared to accept their theory of the pathology of that condition I still adhere to the opinion that there is a specific disease or group of diseases which is characterized by (*a*) fever, slow pulse, severe headache, sternal pain, and a patchy pneumonic consolidation with a characteristic radiological appearance; (*b*) failure to respond to penicillin and sulphonamides; (*c*) rapid response to aureomycin and chloromycetin; (*d*) a high titre of cold agglutinins and in many cases agglutination of the M.G. streptococcus.

It may well be that cold agglutinins occur in other conditions—e.g., infective mononucleosis—but I have yet to hear of any condition in which the cold agglutinins have so high a titre. Reimann (*Medicine*, 1947, **26**, 177) would not accept a titre lower than 1:32. In my small series it varied from 1:256 to 1:1,280. All throat swabs taken showed non-specific results and all sera showed insignificant reactions to the known viruses.

In my opinion any further evidence in the elucidation of this syndrome must largely come from workers in the field, the general practitioners, who alone are in a position to study the epidemiology of such a condition, since few cases are admitted to hospital.—I am, etc.,

Northwood, Middlesex. DUDLEY M. BAKER.

Erysipeloid of Baker-Rosenbach

SIR,—I was interested in Drs. J. E. L. Price and W. E. J. Bennett's article (November 3, p. 1060) on the erysipeloid of Rosenbach (or, more accurately, Baker–Rosenbach, as suggested by Roederer and Lanzenberg[1]). It is, of course, far from a rarity. It is a common mistake for our more academic colleagues to assume that because they seldom see or read about a disease it must therefore be rare; McNeill Love[2] even suggests that this is due to frequent misdiagnosis. The fact is that erysipeloid is well known to many practitioners who treat and cure their patients without reference to hospital.

The clinical features are pathognomonic, and the disease ranks with mongolism, pink disease, etc., for, having once been seen they are never forgotten. Unfortunately Price and Bennett have omitted to mention the single most important clinical feature, dismissing the colour of the lesion as "dusky," which just means dark coloured. The lesion is a dusky reddish purple plum colour which is unmistakable. The patient confirms this subacute appearance with the evidence that it has been present for one or more weeks, the long stage of invasion excluding a pyogenic infection. The satisfaction that Price and Bennett get from "subjecting the patients to biopsy" is derived more simply from discovering an occupational hazard in most cases. Whilst severe pain may be present and such cases are more likely to reach hospital, it is misleading to suggest that this is a feature. The patient more often says, "I'm sorry to waste your time with this, but . . ." "It's been so long, my husband told me to come," etc., statements not indicative of severe pain. Several times I have noticed erysipeloid in the fingers of friends or patients seen for something else. The discomfort may be trivial. Itching may be prominent.

The widespread saprophytic nature of the erysipelothrix is further suggested by the fact that, although erysipeloid is commoner in those handling meat and fish, it also occurs in greengrocers. I have seen two such cases, and Iselin[3] makes this point. An inquiry in Covent Garden would be interesting. The shops euphemistically self-styled, and referred to by Price and Bennett, as "Continental butchers" were known as "Bonzo's butchers" the day before the ban on horse-meat for human consumption was lifted. As long as a horse is worth more to the knackerman than as a horse, erysipeloid is the least one can wish on these vandals. If I am correct in supposing that the "Continental butchers" handle horsemeat, it is surprising that Sneath, Abbott, and Cunliffe could find only one reference to "isolated infections" in the horse in the veterinary literature.

In my experience seven daily injections of 600,000 units of procaine penicillin are curative and enough to prevent a relapse. Sulphonamides are unnecessary, and it is distressing to read that Price and Bennett still use sulphadiazine, especially dangerous when entrusted to an out-patient. The risk of anuria is too great to permit any other choice than sulphamezathine (which is so innocuous that it is becoming more of a food than a medicine). Efficient and early treatment is desirable, as articular stiffness is sometimes a troublesome sequel of erysipeloid (Buzello[4]). The patient may be simply reassured that two to three weeks will usually see the end of his symptoms. Price and Bennett's statement, "Thus, of the 15 patients of whom we have full details, 7 (47%) were symptom-free within six days, and 11 (73%) within 12 days," must have brought an extra loud blast from Mr. Grant Waugh's trumpet.

Price and Bennett have done a service in again drawing attention to erysipeloid, but the implication that it is either uncommon or widely misdiagnosed cannot be allowed to pass unchallenged.—I am, etc.,

Worcester C. ROMER.

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2 Love, R. J. McNeill (1949). *British Medical Journal*, **2**, 1411.
3 Iselin, M. (1940). *Surgery of the Hand*, p. 154. London.
4 Buzello, A. (1935). *Report to the 7th International Congress of Industrial Accidents*, Brussels, p. 517.

Plain Words

SIR,—The neglect of the linguistic evolutionary point of view occasions Dr. B. Isaacs (October 27, p. 1032) unnecessary heartache. Language cannot be regarded as a museum piece like the stone axe, the bronze hatchet, and the bow and arrow. It is something very much alive, growing and expanding and constantly escaping from those semantic, syntactical, and accidencial constraints in which the linguistic anatomist of the grammarian would contain it. Such a person is inclined to look to what words *are* rather than what they *do*.

The purist or would-be purist in language is invariably vulnerable on the very ground he so stoutly champions. Thus to one like myself, who is not a purist and who zealously and habitually eschews the sesquipedalian utterance in favour of those cogent and pungent brevities which approximate to basic English, such an opening sentence in Gowers's *Plain English* as, "This book was written at the invitation of the Treasury," or Isaacs's, "But I should like to conclude with an example . . ." would have been written, "The Treasury asked me to write this book," and, "I want to end with an example. . . ." It is a pity that Dr. Isaacs chose Gowers's *The A B C of Words* as a model, for, apart from its being a very poor imitation of Fowler, a worse example of a book which falls into many of the errors it exhorts others to avoid could scarcely be found—and that right from the first paragraph, which is uneven in style, alternating between mandarin English and the colloquial, which begins with the passive and then swings over into the active, which is verbose to the extent of being

easily condensed into half, at least, of its present size, and whose meaning could be more easily grasped by the judicious employment of inverted commas. Dr. Isaacs's letter shows similar peculiarities: apart from its unevenness and colloquialisms foreign to the august columns of the *British Medical Journal*, he, for instance, uses "penchant," a word which has never become naturalized in the English language, attacks "obstetric colleague," which satisfies the linguistic canons of the schoolmarm, and the employment of "follow-up" as a verb, adjective, and noun as if that were either something new or reprehensible in English, whereas in the hands of Shakespeare and the lesser lights it was one of the advantages, even glories, of English, a tradition which doubtless Dr. Isaacs carries on in a humbler way on those occasions he *parks* his car in a car-*park* and gets a chit from the car-*park* attendant.

Dr. Isaacs (and Sir Ernest Gowers), ignoring the evolutionary linguistic point of view, does not seem to see that many of what he considers the garish and discordant linguistic practices and innovations of to-day will become the staid philological respectabilities of to-morrow, just as "Good-bye" must have at one time sounded a very slangy rendering of "God be wi' you" and "narrate" stigmatized as a Scotticism by Johnson.

Let Dr. Isaacs take heart from a sentence from the magnificent peroration which ends Bradley's *The Making of English*—"In the daily increasing multitude of new forms of expression, even though it may be largely due to the unwholesome appetite for novelty, there must be not a little that will be found to answer to real needs, and will survive and be developed, while what is valueless will perish as it deserves."—I am, etc.,

Shotts, Lanarkshire. R. GOOD.

More Blasts on the Trumpet

SIR,—Mr. W. Grant Waugh's trumpet blast (November 3, p. 1088) is indeed timely. But he needs a surgical, not a musical, instrument—a lithotrite—in order to eradicate the calculus which many of us find so painful. An example of the cerebral exaltation—I prefer the word conceit—to which he refers occurred at a recent medical meeting when, after three short papers had been read by mature and much-respected clinicians, the fourth speaker, a young medical statistician, opened with the remark, "You have heard the previous speakers with great interest; I will now give you the facts."

I think it would be fair to say, Mr. Editor, that most of your readers have little interest in higher mathematics. We open our journals in a mood of quiet enjoyment and relaxation, hoping to find something to help us in our pursuit of humanism, of the *art* of medicine. If the mathematically minded must burst into print, then let their jargon be published elsewhere, and not in our clinical journals.—I am, etc.,

Maidstone. F. TEMPLE CLIVE.

Educating the Public about Cancer

SIR,—I read with great interest the letter from Dr. James F. Brailsford (November 10, p. 1154), the main object of which, I gather, is to criticize in general education of the public concerning cancer, and in particular my article in *Family Doctor*. His first criticism is of my use of the word "cure." I agree it is very difficult to define a cure, but this applies to other diseases besides cancer. For example, when I was 14 years of age, before *x* rays were discovered, I suffered from a prolonged and obscure illness, the cause of which was accidentally discovered to be tuberculosis when my heart was *x*-rayed at the age of 60. I consider that I am cured, but the scientific proof of that belief must wait until I am dead and serial sections of my whole body are examined to exclude the presence of a single living tubercle bacillus.

The same is true of cancer, but even most intelligent patients consider that when there is no sign or symptom of a disease they are cured. The question of what yardstick of time should be used to denote a cure in the case of cancer is a debatable point, but five years without sign or symptom seems to me to be a very convenient one.

Dr. Brailsford's idea that women have an intuition about the presence of cancer of the breast is interesting, but surely he does not advocate mastectomy in such cases before there is any other evidence. If all these intuitions are correct some of the growths must develop very slowly, as there are patients whom I reassured more than 20 years ago, who so far have developed no further evidence of the disease.

The object of some of the paragraphs in the letter, such as the criminal omission to do a rectal examination, freedom of the Press, the tactlessness of some doctors, etc., is a little difficult to unravel, but I must take exception to one phrase—propaganda of fear. This suggests that my education campaign is based on producing fear. Fear is a justifiable weapon to use in the case of a preventable disease—e.g., diphtheria, venereal disease, etc.—but if used in cancer it would defeat the very object it has in view—namely, earlier diagnosis. The whole object of cancer education in this country is to diminish fear, which—and I gather Dr. Brailsford agrees—is the main stumbling-block to earlier diagnosis.

Everybody will agree that when a cure (Dr. Brailsford uses the word in this connexion) is found for all types of the disease, and in all its stages, cancer education will no longer be necessary. Meanwhile, what does Dr. Brailsford propose to do? Surely he is not satisfied with the *status quo*?—I am, etc.,

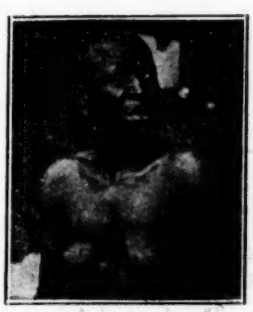
London, W.1. MALCOLM DONALDSON.

SIR,—The article in *Family Doctor* which Dr. James F. Brailsford criticizes (November 10, p. 1154) was written by a recognized authority in this field, who freely admits that treatment fails in 25% of early growths. As an expert his results are perhaps better than the general average; but if only 10% were cures the effort would be worth while. But what is "cure"? We cure all manner of disorders, but have never agreed upon a satisfactory definition of the term. Some maintain that we do no more than relieve. Yet surely a man or woman who is happy, interested, and in reasonable bodily comfort 5, 10, or 15 years after operative or other treatment of early cancer may be said to have achieved something remarkably like the popular notion of a cure.

There is much that can be done about cancer if its presence is detected early, and this presupposes some awareness among the public through carefully designed cancer education. Given a little more knowledge the failures might have sought help sooner and would perhaps be listed in the other column. The opposing view, which Dr. Brailsford seems to endorse, is that we should sit tight and do nothing since nothing's no good. Of these opposites but one can be right, and there can be no doubt about which is the more rewarding.—I am, etc.,

Bognor Regis. H. D. LIVINGSTONE-SPENCE.

Gynaecomastia in a Leper



Tamale, Gold Coast.

SIR,—The history of the patient in the photograph is as follows: He is about 40 years, married, and has one daughter aged 12. He developed leprosy nine years ago. Three years later he developed gynaecomastia. His genitals are normal. Dr. C. Bowesman has a similar photograph of a case seen in the Gambia. He remarks that it is fairly common in lepers.—We are, etc.,

J. C. V. MURPHY.
M. P. BROWNE.

Malaria

SIR,—The opportune letter by Sir Philip Manson Bahr (October 20, p. 969) is a further valuable contribution to many he has made over a number of years in calling attention to the dangers of subtertian malaria in non-immunes. Two points in his letter call for special comment.

In most textbooks the incubation period is given as between 10–14 days. Kitchen (1949), in Boyd's *Malariology*, gives a mean incubation period as 13.1 days. Sir Philip points out, however, that fever may develop 7–10 days after infection. It is not generally realized that the incubation period in subtertian malaria may be as short as five days. On several occasions in malaria-therapy with *P. falciparum* I have found parasites in the peripheral blood on the fifth day after infection, accompanied by fever. This means that at least some pre-erythrocytic parasites complete their development in parenchyma cells of the liver in three days if, as I assume, at least one generation of the erythrocytic cycle is necessary to cause fever.

During the war I found subtertian malaria parasites in a man who had spent only 24 hours in West Africa. He had gone there by air and returned the following day. When I saw the patient he had been ill for about a week and over 3% of his red cells contained *P. falciparum* parasites. Among other reasons why malaria was not suspected were that he had spent only one night in Africa and that he had had no rigors. It does not take a mosquito more than a few seconds to inject sporozoites (it is not necessary for the mosquito to withdraw blood in order to transmit infection)

Rigors are a dominating feature in *P. vivax* malaria, but they are uncommon in subtertian malaria, and therefore their absence should never be considered as a reason for ruling out malaria. Indeed, in patients ill with fever from or in a malarious region the absence of rigors should be considered as a serious manifestation indicating subtertian malaria. When non-immunes suffering from subtertian malaria develop rigors a careful search will usually reveal the presence of developing forms of the malignant tertian malaria parasite and should always be regarded as a danger signal for immediate and drastic therapy. When *P. falciparum* malaria parasites are numerous in the peripheral blood during the height of an attack of fever it indicates that there are multiple generations, each group segmenting at different times, which is clearly seen by the temperatures, the fever being quotidian or double quotidian instead of the classical type of fever as indicated by the term malignant *tertian* malaria.

Finally, well-stained blood films with one of the Romanowsky modifications are essential in order to demonstrate clearly the tiny ring forms of the subtertian malaria parasite, and especially "accolé forms," which occupy only about one-tenth of the diameter of the red blood corpuscle. In acute primary cases of *P. falciparum* malaria the merozoites in the peripheral blood are much smaller than those of the same strain of parasite in chronic cases, when the ring forms may occupy one-quarter and sometimes nearly one-half of the red cell. These large *P. falciparum* parasites may easily be mistaken for *P. malariae* parasites and may show one or two grains of pigment in the cytoplasm.—I am, etc.,

Malaria Reference Laboratory, Epsom, Surrey. P. G. SHUTE.

SIR,—Having been written by such an authority, the article on malaria by Sir Gordon Covell (October 27, p. 1021) must command wide attention and respect. It is therefore of great importance that the doctrine in it be sound. Sir Gordon dismisses the intramuscular injection of quinine in emergency as "apt to cause necrosis and abscess and said to predispose to tetanus." No one will dispute that abscess and necrosis have sometimes followed intramuscular injections of quinine. There is a striking photograph of an example of the latter in Manson's *Tropical Diseases*, but, far from condemning the treatment, Manson gives advice on its right use. It is also undisputed that on occasions tetanus has followed intramuscular quinine, but *post* is not always *propter*, and I have never heard the use of catgut in surgery condemned because tetanus has sometimes followed its use in operations.

In many years of practice in a highly malarious country where falciparum malaria abounded and took a high toll of life I have never had the misfortune to see either abscess or tetanus follow intramuscular quinine, but I have seen many a life saved by it, especially where the patients were infants in whom intravenous injection would not have been possible. I have not sufficient confidence that the other drugs mentioned by Sir Gordon have such a quick action as quinine in cases where quick action is called for. This fear of intramuscular quinine is not a new one, and seems to belong to practitioners in India rather than tropical Africa. I have no explanation of this.

May I be forgiven for ending with a personal experience? In 1940 I was very ill at sea with bacillary dysentery and subtertian malaria. Vomiting was very distressing. My medical attendant refused all my entreaties to give me an intramuscular injection of quinine, saying he did not want to give me tetanus. He was persuaded with much difficulty to inject mepacrine after disclaiming any responsibility for the damage it would certainly cause in my gluteal muscles. Needless to say, there was no damage and my malaria was brought under control in due course, but not so quickly as with quinine.—I am, etc.,

H. G. CALWELL,
Late Medical Specialist, Tanganyika Territory.
Belfast.

Chemical Tests for Blood

SIR,—In his interesting letter on "The Cold Light Test" for the detection of blood (November 3, p. 1092), Dr. K. F. Anderson asks for more information about this test. So far as I know the first mention of the use of *o*-aminophthalic cyclic hydrazide in a chemiluminescence test for blood was made in a paper by Specht in 1937 (*Angew. Chem.*, **50**, 155) on the detection of blood-stains for forensic purposes. A good description of this test is given by Proescher and Moody (*J. Lab. clin. Med.*, 1939, **24**, 1183), who find that it will detect haematin in a dilution of 1 in 10^8. The test appears to be of use in medico-legal work, as the solution can be sprayed on coloured materials and surfaces, and any blood-stains present will show by their luminescence.

Like the other substances used as tests for blood—e.g., benzidine—it is a general reagent for peroxidases, and for this reason it is preferable to boil and cool the urine or faecal suspension first to avoid false positives. Proescher and Moody advise acidifying with hydrochloric acid, boiling and neutralizing, and then applying the test. I find that by acidifying before boiling one avoids the loss of sensitivity often found after boiling the untreated solution. I have not had sufficient experience of the test in routine use for occult blood in faeces to give an opinion on its value in comparison with the methods more commonly used. In practice this test is sensitive and reasonably free from false positive reactions. So far as occult blood in urine is concerned there is no doubt that the method of choice is to examine the centrifuged deposit under the microscope.—I am, etc.,

North Middlesex Hospital, London, N.18. A. B. ANDERSON.

Heatstroke in Infant Mortality

SIR,—In Dr. Douglas Swinscow's interesting article on so-called accidental mechanical suffocation of infants (October 27, p. 1004) I was surprised to see no mention of heat-stroke and am reminded of the following case.

While I was visiting a patient at 12.45 p.m. on a warm day in March, 1948, the patient's wife went out to the garden to bring in their two-months-old infant who had been lying in his pram in the sun. She came back immediately to ask me to go out to see the baby, as he was looking "peculiar." I found the baby's clothes wet, but his skin dry and hot. The respirations were about 140 per minute and the heart beat was uncountable. The baby was twitching and squinting and his temperature in the groin was 107° F. (41.7° C.). By removing his clothes and sponging him with cool water I brought the temperature down to 102° F. (38.9° C.) in a few minutes. I then gave him some saline in his bottle and left him quiet and lightly covered. Within an hour he seemed out of danger, but he ran a temperature of

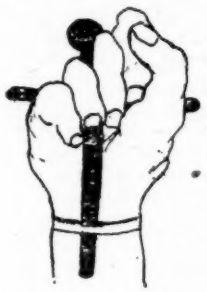
99° F. (37.2° C.) to 102° F. for four days, which I attributed to instability of the heat-regulating mechanism, as I could find no infective cause for the pyrexia and he had been perfectly well before the incident.

If this baby's mother had been half an hour later going to him I suppose he would have been found dead in his pram, and I think it likely that the death would have been attributed to suffocation. Really, however, I think it would have been due to heatstroke through excessive clothing on an unexpectedly warm day. I imagine such accidents have been the real cause of many infant deaths in cradles and cots, and I think the danger of over-heating a very young baby and the ease with which it can be done should be more widely known.—I am, etc.,

Ilfracombe. A. STORMONT

Murder by Spleen Rupture

SIR,—Your annotation on rupture of the spleen (November 3, p. 1077) recalls to my mind an experience of many years ago when I was a ship surgeon in the Far East. A Dutch doctor, in return for some courtesy of mine, presented me with the secret murder weapon used by the Dyaks to produce death by rupture of the spleen.



Enlarged malarial spleen was very common in Celebes, and the weapon was used to strike a heavy concentrated blow over the enlarged area of dullness so as to rupture the spleen and yet show no external sign of violence. The weapon looked like a child's wooden dagger. It was about 8 in. (20 cm.) long and was held in an unexpected way. The cross-bar of the dagger was concealed in the clenched palm of the hand. The knob of the handle protruded forward between the middle and ring fingers; and the blade, so-called, lay over the wrist and up the forearm for about 3 in. (7.6 cm.). This portion was strapped securely round the wrist, and the whole weapon could be concealed easily in the sleeve of the Baju jacket. All one had to do was to approach the unsuspecting victim and make a jab at him below the ribs on the left side. If he had an enlarged spleen it was quite easy to rupture it. It was a fiendish method, much more subtle than the split bamboo, which makes a definite puncture wound. Like the method used by the thugs in India, it was kept a great secret and often completely escaped discovery.—I am, etc.,

London, W.C.1. J. JOHNSTON ABRAHAM.

Ferrous Sulphate Poisoning in Children

SIR,—With reference to the article by Dr. I. O. B. Spencer (November 10, p. 1112) on the danger of ferrous sulphate poisoning of children through the accidental acquisition of tablets intended for adult use, may I make the following comments as a result of long experience in an extensive hospital practice in London?

I agree entirely that to produce uncoated, and therefore unpleasantly tasting, tablets results in a reduction of much-needed medicament taken by patients, in particular ante-natal cases. The reduction in consumption as measured by the drop in demand when the external form of the tablet is changed can be as much as 75%. I think that to attempt the organization of a packed supply on the lines of a number of medicaments now available in strip sealed form would be prohibitive from the point of view of expense on a large hospital scale. An inexpensive aid which is close at hand is to provide *all* tablets in screw-capped bottles. This practice has been rigidly followed in my old hospital in London for more than 20 years, and I am satisfied that children of 1 to 2½ years of age, the age group including almost all this type of accident, can very rarely remove the screw top from a bottle, as normally applied by the average adult, for some considerable time when playing with the container. The rattling sound produced is itself some distraction from the desire to remove the cap. A warning note should be a normal feature of labels on all such bottles.—I am, etc.,

Leeds. JOHN WHITE.

In Praise of Pethidine

SIR,—At a time when pethidine is extensively used for the relief of pain in childbirth, it is highly desirable that any untoward reactions should be brought to our notice, but it is equally important that the drug should not be condemned without full investigation. I agree with Mr. W. G. Mills (October 20, p. 971) that one must think of the entire process of labour before attempting to evaluate the influence of one factor.

I have been responsible for the administration of pethidine, either alone or in combination with "scopolamine," to over 5,000 women in labour. Careful records have been kept, and out of this number there was only one case that showed undesirable reaction. A primigravida, aged 23 years, suffering from active phthisis was given an intramuscular injection of 100 mg. pethidine at three-quarters dilatation. About 10 minutes later an urticarial rash developed on the arm receiving the injection and she vomited once. However, her general condition remained satisfactory and she was delivered of a living child an hour and a half later. Shock has occurred in patients who have received pethidine, but in each case there has been a definite obstetric cause. The incidence of shock in patients given pethidine compares favourably with that occurring in cases not given the drug.

I am quite sure that there are many hospitals which can offer a record of results as satisfactory as the one I put forward. However, the fact remains that a case such as Dr. E. Blanche Butler described (September 22, p. 715) needs careful consideration, and this is a problem that could well be solved by clinician, pharmacologist, and chemist working together.—I am, etc.,

London, W.12. HILDA ROBERTS.

Pregnancy after Vulvectomy

SIR,—The vast majority of cases of leucoplakia occur in post-menopausal women, so that the association with pregnancy is extremely rare.

A woman aged 39 years first attended as a gynaecological outpatient in June, 1946, complaining of increasing vulval irritation over the past six months. She had not been aware of any vaginal discharge. Her menstrual cycle was normal, 3-4/28. She had been married 20 years. She had had one normal, full-time pregnancy 16 years ago, and in the succeeding five years four abortions at three to four months.

On examination she appeared to have extensive leucoplakia involving the vulva and perineum. At one site on the vulva there was fissuring and ulceration. A diagnosis of leucoplakia with possible malignant change was made. A specimen from the vaginal pool revealed a normal vaginal flora; bimanual vaginal examination showed no abnormality. A radical vulvectomy was performed on June 14, and the specimen sent for microscopic examination showed leucoplakia with no evidence of malignancy.

On January 21, 1950, emergency admission to the maternity hospital was requested for this patient by her family doctor on account of a mild antepartum haemorrhage complicating a full-time pregnancy.

On admission her general condition was good; she had no vaginal bleeding after admission and was early in labour. After a first stage of nine hours, the second stage of 20 minutes was terminated by a wide episiotomy, followed by spontaneous delivery of a 5 lb. 9 oz. (2.5 kg.) child. The vulval scar was supple and stretched easily. The episiotomy was repaired in layers and united well. The puerperium was normal. She was seen at the post-natal clinic and again in June, 1950, when she reported feeling well and examination was satisfactory.

After the patient's admission to the maternity hospital, the original sections from her vulva were re-examined, and the diagnosis of leucoplakia was confirmed by another pathologist. The association of pregnancy and leucoplakia is very rare. I can find only one reference to it in recent literature. In 1941, V. B. Green-Armytage reported (*J. Obstet. Gynaec. Brit. Emp.*, 1941, **48**, 524) a case of leucoplakia complicating

a pregnancy and mentioned two other cases. Way has told me of two of his cases in which pregnancy occurred after vulvectomy for severe leucoplakia.

I wish to thank Mr. T. G. Robinson for his permission to publish this case occurring in his unit.

—I am, etc.,

South Shields. AGNES M. STARK

Histamine Skin Tests in Ménière's Disease

SIR,—Dr. Michael Haggie's article (November 3, p. 1057) adds further weight to the view generally accepted in this country that histamine skin tests have little bearing upon the effect of histamine in the treatment of Ménière's disease. (Approximately one-third of the patients proved to have this condition on careful clinical examination are relieved almost completely of the attacks by this treatment.) The skin test is useful in that it gives some indication of the patient's sensitivity to histamine and thus of the dosage required. In my experience the patients who respond to histamine injections respond almost equally satisfactorily to oral nicotinic acid, which has a similar effect of producing vasodilatation, but it is of great importance that the nicotinic acid should be given on an empty stomach so that absorption may be rapid. If the tablets are crushed and taken with a little warm water the patient may experience a satisfactory flush with as little as 100 mg.

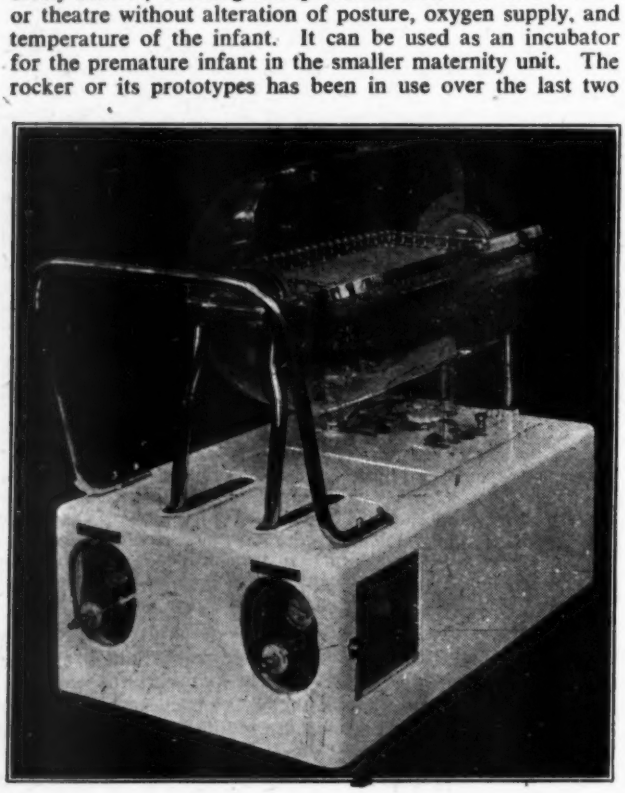
The hypothesis that vasodilatation is of significance in the treatment of Ménière's disease is supported by recent articles demonstrating that cervico-dorsal sympathectomy is effective in controlling the vertiginous attacks.—I am, etc.,

Lincoln. M. SPENCER HARRISON.

A Rocker for Asphyxia Neonatorum

SIR,—The primary object of this rocker is the utilization of the Eve method of resuscitation while affording adequate oxygen and the conservation of the infant's temperature.

We feel that this rocker is an improvement on other types, as it is electrically driven, can be pre-set, and is thus immediately available for use by the medical and nursing staff in any emergency. It has the added advantage that it is freely mobile, allowing transportation from the labour ward or theatre without alteration of posture, oxygen supply, and temperature of the infant. It can be used as an incubator for the premature infant in the smaller maternity unit. The rocker or its prototypes has been in use over the last two years at the Bearsted Memorial Hospital, London, Hillingdon Hospital, Uxbridge, and St. James's Hospital, Balham, where it has proved its value in a considerable number of cases. At the last-named hospital the rocker has been in use or at readiness in 62 out of 500 consecutive deliveries. 50 of these babies (10%) have actually been rocked.



The types of case in which it has been used are all caesarean sections, all assisted breech deliveries, all forceps deliveries under general anaesthesia, and for babies born in blue asphyxia.

The rocker has been used where there was no attempt at respiration, but all the babies had pulsation of the cord or perceptible heart beats. None of the rocked babies with the heart beating failed to revive, although one case of cerebral haemorrhage died four hours later.

The rocker consists of a removable chrome-plated basket containing a foam rubber mattress placed in a "perspex" cylinder. This cylinder rocks from a fixed point, is smooth in its action, and the speed of rocking can be varied from 10 to 20 rocks per minute. Quick access to the baby is available by a release latch which allows the top halves to slide over the bottom half. In the base are the variable speed drive, the control panel, and two standard oxygen cylinders on racks for easy changing. If any cylinder should fail a signal light on the control panel goes out. The rocker is fully protected against static electricity and sparking.

We wish to thank Dr. John Frankenberg for his many helpful suggestions and advice. We are indebted to the consultant staff of the Bearsted Memorial Hospital, to Dr. Joyce Morgan, of Hillingdon Hospital, and to Miss I. R. Bishop, of St. James's Hospital, and also to Mr. S. F. Harrison, who arranged for the rocker to be made by the R.B. Production and Engineering Co., Ltd., Bridlington, Yorks.

—We are, etc.,

London, N.15. D. B. HANDLEY. DIANA HANDLEY.

Bacteriology of Infantile Gastro-enteritis

SIR,—In their interesting article on this subject Drs. I. A. B. Cathie and J. C. W. MacFarlane (October 27, p. 1002) comment, "Our results do not support the idea that the organism we have investigated is causal" (in infantile gastro-enteritis). Without prejudice to the ultimate decision whether strains of *Bact. coli* can or cannot cause gastro-enteritis in the human infant, it does seem possible to place a different interpretation upon the findings reported by the authors. The uncertainty in interpreting infection rate figures arises largely because so many potentially pathogenic bacteria can also thrive as commensals, and the issue is further confused because a symptomatology does not necessarily define a disease.

The symptoms of infantile gastro-enteritis can probably be provoked by several circumstances, including colonization of the gut by organisms to whose effects the host is sensitive. In any series of cases, therefore, the higher the proportion attributable to known causes, the fewer the cases remaining to be explained by a suspected cause, such as in this instance *Bact. coli* O Group 111. In this series, however, no reference is made to other positive findings (although it is stated that the beta type of *Bact. coli* was *not* sought), and so the significance of the total number of cases (264) in the series cannot readily be assessed.

A subdivision of the authors' figures reveals a decline in the incidence of *Bact. coli* O Group 111 among their gastro-enteritis cases during the period of their survey. Thus, if the figures relating to the two periods of time, June, 1949, to September, 1950, and September, 1950 to March, 1951, are taken separately, a difference emerges. 77 of 179 or 43% of cases admitted to hospital in the first period yielded the organism, whereas only 14% of 85 cases admitted in the second period were found so infected. These figures could mean that emergence from an epidemic period was taking place in 1950, and if this were so it would influence the expected frequency of infection in cases and controls. For example, during a recent outbreak of Sonne dysentery a high proportion of all cases of diarrhoea and of their contacts were found to be infected with the prevailing organism, but as the epidemic waned the proportion of diarrhoeas from which *Sh.*

sonnei was isolated fell, though for a time the organism continued to be isolated from numerous convalescents and excreters. It is possible that a similar pattern might apply in the case of *Bact. coli* O Group 111. If this were so, it might explain the fall in the proportion of cases found infected from 43% in 1949–50 to 14% in 1950–1, together with a 20% incidence among controls in the second period. Unfortunately, no controls were examined during the "epidemic" 1949–50 period.

The frequency with which potentially pathogenic organisms are isolated from healthy individuals depends on many factors, including the thoroughness of the search. The authors made an unusually careful search for *Bact. coli* O Group 111, examining 30 colonies from every culture, and it would be very interesting to know if they found the proportions of positive colonies higher among fresh cases than among controls.

When a community is exposed to an infection which has a low symptom rate, or if the duration of the infection far exceeds that of the symptoms, then a very high carrier rate may be found, and indeed *Staphylococcus pyogenes* has been found in 80% of swabs from the noses of some samples of healthy persons. Though commonly so, it is perhaps not axiomatic that if an organism is pathogenic then its incidence among cases of a related symptom must exceed that among symptomless controls. It is conceivable that the picture might sometimes be reversed if the community had a high carrier rate, if the organism could produce more than one clinical syndrome (e.g., osteomyelitis and blepharitis), or if a high proportion of cases with indistinguishable symptoms were being produced by another cause.

If the authors' findings are reviewed with these considerations in mind they do not necessarily exclude a causal relationship between *Bact. coli* O Group 111 and infantile gastroenteritis, and the organism, though unconvicted, remains under suspicion. Should it ever be proved to be pathogenic, the high excreter rates, the cross-infection of 13% of 175 hospital cases, and the 30.7% "positive stool on discharge" rate would come to be viewed with concern. Meanwhile it would perhaps be well not to let scepticism open the door to cross-infection.—I am, etc.,

London, N.W.3. MAIR E. M. THOMAS.

Radiography in Determining the Placental Site

SIR,—Professor J. Chassar Moir and Mr. John Stallworthy having pointed out (October 20, p. 974) the "factual error" made by me in stating that Dr. Frank Reid's most important work on radiography of the placental site was done under their "inspiration," the least I can do is to offer to Dr. Frank Reid my personal apology in the columns of the *Journal*. Furthermore, I have written him a personal letter to this effect. The term I should have employed was "encouragement," the term which Dr. Frank Reid himself employs in the *British Journal of Radiology* (1949, **22**, 664). Here are his words:

"I wish to express my thanks to Dr. F. H. Kemp for the encouragement and constant support he has given me throughout these investigations, also to Professor Chassar Moir, Mr. J. A. Stallworthy, Mr. G. Gordon Lennon, Mr. Hawksworth and the Staff of the Radcliffe Infirmary, Maternity Department. . . ."

No one interested in obstetrics can fail to be impressed by the investigations carried out by Dr. Frank Reid on the identification of the placenta *in situ* by radiography and described by him in the October and November numbers of the *British Journal of Radiology* (1949) under the title "The Radiological Localization of the Placental Site." Personally, I was particularly interested in his commentary on "amniography." "In my opinion, this technique was discarded too soon. In the first place a suitable non-toxic medium could almost certainly be found among the many preparations available to-day." I entirely agree with this statement, and I continued to impress this view upon Dr. McKay until I retired from practice two years after we published our paper in 1933.

And now a word or two on Professor Lennon's letter which appeared in the same issue as that of Professor Chassar Moir and Mr. Stallworthy. Professor Lennon accuses me of greatly over-stating the case, and he quotes my statement: "Vaginal examination excluded, only by radiography can one ensure the degree of exactness in diagnosis essential in making the choice of treatment most suitable for the particular patient under consideration." Here I stated a fact, but I did not say that this degree of exactness had been attained. How could I—long retired from practice—venture on such a pronouncement? It should, however, be possible, and so far as I can judge from recent writings on the subject (vide *Proc. roy. Soc. Med.*, 1951, **44**, 703–718) this goal is yearly becoming nearer of attainment. After all, it is only within the last few years that our obstetricians and radiologists have seriously tackled this problem, incidentally infinitely more difficult than that of estimating pelvic formation and capacity by radiography.

Finally, why qualify the value of radiography in obstetric practice? And why distinguish it as being apart from ordinary clinical methods? It is a clinical method and extensively employed as such to-day by physicians and surgeons.—I am, etc.,

Canterbury. J. M. MUNRO KERR.

Rupture of Rectus Abdominis

SIR,—I was interested to read the article by Mr. Herbert S. Trafford on rupture of the rectus abdominis muscle (November 10, p. 1130), as in the past week I have had the opportunity to operate on a related condition.

A man, aged 77 years, had been confined to his bed for a week with bronchitis. During one severe bout of coughing he experienced a sudden pain low down on the right side of his abdomen and shortly afterwards noticed a mass at the site of the pain. He was admitted to hospital with the provisional diagnosis of strangulated inguinal hernia. On examination there was an acutely tender hard mass 2 in. (5 cm.) in diameter overlying the outer border of his right rectus abdominis. The centre of the mass was 2½ in. (6.25 cm.) above the pubic spine. It had no cough impulse and was still easily palpable when the shoulders were raised.

A diagnosis of haematoma of the rectus sheath was made, but as the alternative diagnosis of strangulated Spigelian hernia could not, with confidence, be excluded, exploration was decided upon. A short paramedian incision was made, and as soon as the subcutaneous fat was divided the rectus sheath was seen to be bulging and blue. On incising the sheath a clot was immediately extruded. Further dissection and removal of the clot revealed that there was a vertical tear 1½ in. (3.75 cm.) long in the fused aponeurosis of the oblique muscles at the lateral edge of the rectus muscle. The tear extended above to the level of the arcuate line (linea semicircularis), and through it the peritoneum, covered only by the fascia transversalis, could be seen. An attempt at repair failed owing to the friable nature of the tissues. It was interesting to note that the acute pain had gone by the next day, presumably due to the release of clot which was under tension.

A comparable case is reported by R. A. Jamieson, *Brit. J. Surg.*, 1949, **36**, 434.—I am, etc.,

Boxmoor, Herts. J. PETT TURNEY.

SIR,—The two articles in the *Journal* of November 10 discussing the condition of rupture of the rectus abdominis muscle were most interesting but described the condition only in women. I do not know what the sex incidence of this condition is, but it appears to be even more uncommon in the male, and therefore a note of such condition occurring in a man may be of some interest.

A man aged 69 had been admitted on April 23 as a case of hypertensive heart failure. He was referred for surgical opinion because it was thought he had developed an acute abdomen. On examination he presented the clinical findings described by Mr. H. S. Trafford (p. 1130), having a hard, fixed, fairly well circumscribed swelling in the left iliac fossa. The mass was tender. It was impossible to tense the abdominal muscles to fix the mass because of the intense pain from which he was suffering. No definite diagnosis was made, but it was thought probable that he had an internal strangulation. It was noted that the blood pressure was 185 mm. Hg systolic and 120 diastolic. The patient looked extremely ill and shocked.

Exploration was carried out, and the findings were those so well described, the rectus sheath having been ruptured. The deep epigastric vessels were intact, but it was seen that there were some small muscular branches still bleeding, and these were transfixed. The rupture had occurred high up in the rectus at the junction of the upper one-third and lower two-thirds. A clot was taken out, the rectus sheath sutured, and a drain left in the cavity.

The wound took some time to heal, but eventually did so satisfactorily.

The points that I would like to make are the extreme difficulty in making a diagnosis because of the tenderness of the abdominal wall and intense pain, and the fact that this condition does occur in males, associated in this patient with hypertension.—I am, etc.,

Wordsley, Worcs. M. HERSHMAN.

Urinary Chloride and Potassium Deficiency

SIR,—Dr. W. H. Taylor (November 10, p. 1125) has pointed out that the urinary chloride concentration is not always a sufficient guide to the need for saline therapy. This is particularly true in post-operative cases, which may have a high urinary but low plasma chloride content. It may perhaps be pointed out that even if the plasma chloride is known to be low this is not necessarily an indication for "saline" (NaCl) therapy.

After an abdominal operation patients commonly become potassium deficient, though this is not always reflected in the serum level of potassium. They become potassium deficient because:

They suffer an unavoidable loss of potassium through the bowel and an unavoidable loss of potassium by aspiration of intestinal contents;

They are maintained on potassium-free parenteral fluids;

They continue to lose potassium in the urine in spite of potassium deficiency.

Potassium deficiency tends to produce low chloride and high CO_2 values in the plasma. Chloride administration does not correct this hypochloraemic alkalosis and excess chloride is simply excreted in the urine. Hence potassium deficiency would account for some of the cases in which a low plasma chloride is associated with a high urinary chloride content.

The only way to show definitely that a patient lacks potassium is to show that he retains an excess of administered potassium. If, however, a potassium deficiency can be reasonably inferred, on the basis of the history, serum values, and E.C.G. changes, then the treatment of these patients is not to give more chloride as "saline," but to give potassium (D. C. Darrow and E. L. Pratt, *J. Amer. med. Ass.*, 1950, **143**, 365, 432). The solutions we have used contain 2.7 or 3.7 g. KCl per litre. Although parenteral potassium must be given cautiously because it can be lethal, there is no point in giving it homoeopathically as Ringer-Locke solution.—I am, etc.,

Oxford. PAUL FOURMAN.

Fantus Estimation of Urinary Chloride

SIR,—Dr. W. H. Taylor's article (November 10, p. 1125) has two main themes: (*a*) the inaccuracy of the Fantus (1936) test; (*b*) scepticism regarding urinary chloride estimations, even when accurate, as a guide to treatment. He devotes the first and largest part of his article to the Fantus test, but concerning the second theme limits himself to a few disparaging references and the conclusion that urinary chloride alone should not guide treatment. Is this not an illogical order of thinking? Surely, if urine chloride estimations are undesirable they had better be scrapped, and defects or merits of any particular method become irrelevant. Perhaps I may be allowed to reverse the order and deal first with the more fundamental subject.

VALUE OF URINARY CHLORIDE ESTIMATIONS

Let it be granted that: (i) Such estimations should not be the sole guide to treatment. It would, indeed, be an odd clinician who would let any single observation control treatment without consideration of all the circumstances of the case as a whole. (ii) Blood estimations and other relevant estimations should be done if facilities are available and *if time permits*. In many of these cases what is done quickly may be of much greater value than what is done a few hours later. (iii) Urine sodium estimations would be better if facilities for making them are available. In my Croonian lectures (Marriott, 1947), from which Dr. Taylor quotes, I said: "Sodium ions are the most important. . . . A similar simple quantitative test (to the Fantus test) for sodium would be even more valuable if it could be evolved." At that time flame photometers were not available, and even now they are confined to a few institutions.

Urinary chloride estimations are of great practical help because: in the *majority* of cases of salt depletion they reflect the body's needs; urinary estimations are often more sensitive than plasma estimations (in most cases of salt depletion urine chloride drops below 1 g./litre long before there is a significant fall in the plasma chloride (Sanchez-Vegas and Collins, 1946). Plasma estimations are, of course, most valuable but are also liable to errors of interpretation. They are measurements of *concentrations*, and adjustment mechanisms frequently preserve near-normal concentrations when *total amounts* are more than doubled or nearly halved (Stewart and Rourke, 1942; Abbott, 1946; Marriott, 1947). The practical importance of urinary chloride estimations is that information is more easily and quickly obtainable than from blood determinations.

Urinary chloride estimations are capable sometimes of misinterpretation, but the fact that a test is not 100% accurate as an index does not mar its usefulness. Most tests are capable of misinterpretation under certain circumstances. Proteinuria does not necessarily indicate nephritis. Glycosuria may not mean diabetes. Are we, therefore, to give up testing urine for protein and sugar? Urinary chloride limitations need definition, and in publications more recent than Dr. Taylor quotes (1950, 1951) I have made an effort to do so:

"Chloride may fail to appear in the urine or may be below 3 g. per litre when salt retention and not depletion obtains. This occurs (*a*) when there is renal damage, slight or severe, and temporarily in the immediate period following anaesthesia and operations; (*b*) when there is cardiac failure or hypoproteinaemia.

"Chloride may be present in urine in excess of 3 g. per litre and yet there may still be a serious degree of extracellular electrolyte depletion. This occurs (*a*) in Addison's disease; (*b*) when sodium chloride is being administered to patients who have lost sodium ions markedly in excess of chlorine ions, as may occur when the secretions lost are derived from beyond the pylorus—that is, fistulae and diarrhoea. Denton (1949) has reported the case of a patient who, for 45 days, lost 2-4 litres daily from a duodenal fistula. The fluid contained twice as much sodium as chlorine, but the urine, during prolonged saline administration, contained twice as much chlorine as sodium and 6 g. of chloride per litre was present when there were still marked symptoms of secondary dehydration."

These exceptions occur in a *minority* of cases. Better definition of limitations will come as knowledge grows. Regarding chloride retention after trauma and operation, it is just possible that the kidneys are wiser than we are.

Warren, Merrill, and Stead (1943) showed that after injury there may be a shift of fluid from the plasma to the interstitial spaces, due to protein leakage from damaged capillaries. The fall of plasma volume produced serious oligaemic circulatory failure. They found saline administration beneficial in that the total increase of extracellular fluid volume, and tissue tension, tended to restore plasma volume and the circulation. It may be that sometimes the body needs an increase of total extracellular fluid by plasma or saline transfusion, subject to watch for pulmonary oedema. The possibility merits consideration before too dogmatic conclusions are drawn on the infallibility of blood estimations and the fallibility of urine figures.

ACCURACY OF FANTUS TEST

Let it be granted that urinary chloride should be estimated by more accurate methods if facilities are available *and time is not lost*. The merits of the Fantus test are that it takes 2 min. to perform and the apparatus and reagents can be carried in a Record syringe box 4½ by 2½ by 1¼ in. The test is sufficiently accurate for practical purposes, and should not be discarded until some better bedside

test can be substituted. Publications confirming its value have been made by Van Slyke and Evans (1948), Paine and Duff (1949), and Black (1950). If a reaction sets in against it, before a better bedside test is substituted, more lives will be lost than would be lost from errors in consequence of its use. Its reliability has been checked by biochemists of the Courtauld Institute of the Middlesex Hospital. Mr. Barrett in 1941 and Mr. Rose in 1951 reported that with freshly passed urine of the *p*H range likely to be met the error did not exceed 1 g./litre when chloride was low—i.e., 0–5 g./litre.

Dr. Taylor's main objections are four:

(i) Urates might make at most an error of 0.7 to 1.4 drops. Even if maximal, such an error is too small to matter, and does the maximum concentration he *assumes* frequently occur?

(ii) Ammonium carbonate, formed from urea, may cause an error up to 2 g./litre if urine is left standing for 24 hours—i.e., until it goes bad. By such time the result would be so belated as to be valueless in any case.

(iii) Errors are likely to be made by inexperienced nurses, students, and house-officers Of course, inexperienced individuals can make a mess of any test, but not of so simple a one if properly taught.

(iv) Regarding his criticism of the test in practical use, he admits that only 0–5 g./litre is of consequence. Therefore I will confine my remarks to his errors within this range. He quotes: "Marriott (1947) considers that in concentrated urine, with a specific gravity of more than 1020, less than 3 g./litre (of chloride measured as NaCl) suggests (salt) depletion." Later Dr. Taylor states that two out of 26 urines, with less than 1 g./litre, showed 2–3 g./litre. Hence, 24 showed 0–2 g./litre and even the whole 26 came within my definition of abnormally low chloride—i.e., even if the test was as inaccurate as he tries to show, which it is not, it is satisfactory for practical purposes. The errors in his table relating to urines containing 0–5 g./litre seem to have been errors on the high side. Was the potassium chromate used contaminated with chloride, as can easily occur from impurity or from contamination by imperfectly washed test-tubes or pipettes? In my lecture, cited by Dr. Taylor, I specifically warned against this possibility and advised that a preliminary control test with distilled water should always be done. Was it done in his cases?

In conclusion, may I briefly allude to Dr. Taylor's adverse implications regarding schemes of treatment put forward by Black (1950) and myself (1947). My scheme was probably very imperfect, though I tried to improve it in later, unquoted, publications (1950, 1951). Criticism of it does not worry me from a personal point of view. It is possible to over-simplify advice regarding treatment, and those of us who have given such advice have probably been guilty of this error. At the same time, it is also possible to over-complicate issues. The majority of patients, and they are many, suffering from disorders of water and electrolyte balances are urgent cases whose lives are in jeopardy. Decisions about their diagnosis and treatment have often to be made in patients' homes or in hospitals at nights or week-end when the help of biochemists may not be available. It is unfortunate if the impression should prevail that there are so many pitfalls that it is safest to do nothing. Dr. Taylor's article contains no positive help at all to the inexpert. Negative criticism is not difficult: the attempt to give positive guidance in comprehensible form is much harder. Dr. Taylor would put us all in his debt if he would attempt the task.

I wish to thank Dr. D. N. Baron, Professor A. Kekwick, Mr. L. P. Le Quesne, and Mr. C. F. Rose for helpful advice. They are not, of course, responsible for the views expressed.

—I am, etc.,

London, W.1. H. L. MARRIOTT.

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R.M.B.F.

SIR,—As only a few weeks remain before Christmas Day, I would like to remind your readers of our Christmas Gifts fund in the hope that those who have not sent their contributions will now do so quickly. We try to make the distribution of gifts some days before Christmas so that the recipients may have the money in time to make their purchases. I appeal earnestly for donations, which should be marked "Christmas Gifts" and sent to the Secretary, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15.—I am, etc.,

London, S.W.15. FRANK JULER.

POINTS FROM LETTERS

Sweetening Agents

The secretary of the Soft Drinks Industry Co-ordinating and Advisory Council writes to say that, contrary to the impression given in the article "Chemical Manipulation of Food" (*Journal*, October 13, p. 863), neither dulcin nor P 4,000 is used in the preparation of soft drinks in Britain.

Mental Calculation of Injection Quantities

Dr. ANTONY M. GREEN (Umtali, Southern Rhodesia) writes: I have frequently found that nursing staff have difficulty in calculating the fractional dose to be given from a tablet of larger dosage. The calculation is not exactly easy for one whose mathematics is poor, and nurses generally dislike admitting that difficulty exists: as a result the quantity actually given is, I fear, too often arrived at by guesswork. I would like to draw attention to the following scheme by which any such calculation can easily be worked out mentally. To give 1/6 gr. from tablet of ¼ gr.: dissolve ¼ gr. in 6 min. and give patient 4 min. (or more easily as a multiple, dissolve in 12 min. and giving 8 min.). Again, to give 1/13 gr from tablet of 1/8 gr.: dissolve 1/8 gr. in 13 min., give patient 8 min.; and to give 1/150 gr. from 1/100 gr.: dissolve 1/100 gr. in 15 min., give patient 10 min. In our hospital here the staff have found this method very helpful.

Bittner's Mammary Tumours in Mice

Dr. J. P. MCGOWAN (Aberdeen) writes: . . . I do not know what Professor Bittner's present views are regarding the cause of the condition: formerly he was of opinion that in all likelihood the agent was a virus. Because of this I repeat the statements made on this subject in my letter in the *Journal* of February 4, 1950 (p. 308), substituting, however, the more apt term "autocatalytic enzyme" for that of "hormone" employed there. It is highly probable that normal milk secretion depends to a large extent on the action of such an enzyme, and that the mammary tumours in mice are to be regarded not so much as tumours as a secretion of very abnormal milk, produced under the influence of a very abnormal enzyme of similar type and activity, the so-called "milk factor," which has made its appearance through harmful recessives becoming dominant during and because of the intensive inbreeding practised.

Cysts in the Surgery

Dr. J. L. KEARNS (London, W.12) writes: I think a lot of time in hospitals is lost in treating ganglia of the wrist and ankle, or Baker's cyst at the back of the knee, which can be treated in the surgery. Having tested for translucency, introduce a small trocar and cannula (No. 3, say), press out the fluid or glue as the case may be, and introduce from a syringe through the cannula a few ml. of "ethamolin." A second aspiration and injection may be necessary. If the stem of the injecting needle and syringe is collared by a tiny rubber ring the ethamolin goes in quite easily and without introduction of air. Prepatellar bursitis of the knee has not yielded so much success.

Registered Drug Samples

Dr. E. B. COWAN (Renfrewshire) writes: On several occasions within the past few weeks I have been called out of my bed at 7.30 a.m. to sign a postman's counterfoil for a sample package of drugs. There is no doubt about the reception which would be accorded to a drug traveller having the temerity to call on a doctor at that time in the morning, but by simply registering an envelope containing a few pills the postman is deputed to do the dirty work. Could it not be made a rule that registered sample packets must not be delivered with the first post? The fact that the packet is usually labelled "Medical Sample" should make it a comparatively simple matter to arrange this. It has struck me as futile that it is possible to register an unsealed packet containing drugs if such registration is intended to prevent the contents falling into unauthorized hands.

Obituary

CHARLES DONOVAN, M.D.

Lieutenant-colonel, I.M.S.

Colonel Charles Donovan, whose death at the age of 88 we recently recorded, was a student at Trinity College, Dublin. He graduated M.D. in 1889 and entered the Indian Medical Service as surgeon two years later. During his early years in India Donovan served on the North-West Frontier with the Tirah Expeditionary Force, taking part in the action at Dargai, and in the operations in the Bara Valley, receiving the India Frontier Medal with two clasps.

After the customary two years' military service, Donovan was posted to Madras for civil employment, and was soon appointed to the professorship of physiology at the Madras Medical College, an appointment which he held until retirement. At first the appointment of second physician at the General Hospital, a post providing abundant clinical material, was an additional charge, but after a few years he became superintendent of the Royapettah Hospital, which carried with it responsibility for the medical care of Government servants living in the third district of Madras City. This hospital, with 80 beds, was probably more suited to Donovan's independent character, and, in the days when special research hospitals were unknown, Royapettah under Donovan's administration amply filled that role. Sir Rickard Christophers has already written (November 10, p. 1153) of the love and regard which he inspired in his students at the Medical College. This characteristic was equally evident at Royapettah, where his staff gave him wholehearted support in his search for new truths.

The writer of this note experienced this loyalty and affection and gained further evidence of Donovan's dynamic personality when he was for a short period in acting charge of the hospital. The occasion itself was characteristic of the man. He was convinced that carriers of many of the tropical diseases prevalent in Madras Residency were to be found among the denizens of the jungle, and he spent his holiday collecting blood slides to prove the existence of monkey malaria. On arrival at the hospital, my first visit every day was to the clinical laboratory, where a collection of small birds and animals which had fallen victims to the hunting enthusiasm of the staff during the previous 24 hours was laid out. By the side of each was a blood slide for my examination. The whole staff took part in this research orgy, and the stained blood slides prepared by the matron, the ward-servant, or even the sweeper were as good as Donovan's own, and these were very beautiful indeed.

Donovan's work and his discovery of the causative organism of kala-azar were wholly the result of individual enterprise, dating from the earliest days of his service and before organized research or special research institutes existed in India. It is probable that his direct and outspoken character was better suited for the private laboratory, but he was never jealous of other workers, and was always friendly and frank about his own work, which he never published until he was sure of its accuracy. Donovan was a senior officer of the Service when the writer joined the Madras Civil Medical Department, and he and other young officers of those days remember with gratitude the many kindnesses and hospitality which he and Mrs. Donovan lavished on them.

Donovan's artistic talents and his knowledge of lepidoptera gave him a very full and interesting life after his retirement from the Indian Medical Service in 1920.

Professor A. S. Mannadi Nayar, additional medical adviser to the High Commissioner for India, has kindly sent us the following appreciation: Colonel Donovan was a characteristically individualistic artist. He was the only professor who entered the lecture-room with the black gown on accompanied by his assistants. He taught only the fundamentals, and that in an unforgettably impressive way, profusely illustrated by graphic diagrams, so beautifully drawn by himself. He entered the wards also in a dramatic way, attended by his assistants, nurses, and students. His remarkable bedside clinical teachings were based on physiological principles. He spent hours on microscope work and stimulated his students to do likewise and also to make full use of laboratory facilities in clinical diagnosis. He encouraged the students to develop an inquiring mind and was one of the pioneers in Madras to promote and encourage research in medical science. He was a remarkable personality who won the hearts of all the students and members of the staff of the college by his frank humour, ready wit, true understanding, and genuine sympathy. He was loved and respected by the students and staff alike, whose real friend he was. He retired from Madras medical institutions in 1920, an inspiring professor, an inquiring physician, an original teacher, and a great scientist, whose name will ever be remembered by students of medicine for his discovery of Leishman–Donovan bodies.

E. B. DOWSETT, D.S.O., M.R.C.S., F.D.S.

By the death of Mr. E. B. Dowsett on November 13 the British Dental Association and Guy's Hospital have suffered an irreparable loss. Although he had reached the age of 76 he had not appeared to change in twenty years, and he was often described as "the man who never grew older."

Ernest Blair Dowsett was educated at St. Dunstan's College, Catford Bridge, and he entered the dental school at Guy's in 1895 for the clinical part of the L.D.S. curriculum, on the completion of his period of training in dental mechanics. He obtained his L.D.S. diploma in 1897, and continued his studies to obtain the conjoint diploma of M.R.C.S., L.R.C.P. in 1899. In 1947 he was elected to the Fellowship of the Faculty of Dental Surgery. Shortly after qualifying he was appointed to the junior staff of the dental school, and for some years was tutor of revision classes for the final L.D.S. During this period he established a reputation as a teacher that was never surpassed. "Dowsett's Notes" (*Dental Surgery and Pathology Notes*) were read in every dental school in the country, and passed through many editions. In 1910 he was appointed assistant dental surgeon and in 1919 dental surgeon to the hospital. He held this appointment until 1935, when he retired under the age limit and was appointed to the consulting staff.

For many years Dowsett was in charge of the teaching of dental histology, and did much original work in this branch of study. Later he lectured in dental mechanics and dental surgery. He was a member of the Board of Examiners in Dental Surgery of the Royal College of Surgeons and other bodies. During the last war he was invited to return to active duties at Guy's, and did so for five years, taking his full share in teaching

and operating. Shortly after his appointment to the consulting staff he became one of the governors of the medical school, and in July, 1948, under the new charter, was appointed a member of the council of governors of the medical school. He still held this appointment at the time of his death.

Dowsett was a member of the British Dental Association for the whole of his professional life, and gave much time to the affairs of its Metropolitan Branch, becoming its president. For many years honorary treasurer of the association, in July, 1951, he was elected president—the climax of his career—but he did not live to complete his term of office. There had been a serious illness in November, 1950, and his relations and friends greatly feared he would not be strong enough for the endless work and responsibility the presidential chair would demand. He was also a former president of the Odontological Section of the Royal Society of Medicine, and chairman of the Dentists' Provident Society.

In his younger days Dowsett was keenly interested in all forms of sport and played lacrosse for Kent. The writer remembers, and many others will do so, the delightful tennis parties at his home at Walton-on-Thames, and also his great love for the river. His other great interest was the Territorial Army. For some time before August, 1914, he commanded the 6th London Field Ambulance. Shortly after the outbreak of the war he was appointed A.D.M.S. of what eventually was to become the 60th (London) Division, and held this appointment until the Armistice. Later he was appointed D.D.M.S. 20th Corps until he was demobilized with the rank of Colonel A.M.S. He served with his division in France, Macedonia, and Palestine, was awarded the D.S.O., and four times mentioned in dispatches. In private life he was a perfect friend and companion, always ready to help another. His modest demeanour covered and disguised a keen mind and an ability of high order. His many friends and admirers will miss him sadly. The gap he has left will not be filled readily, for in his case death seemed so untimely. All his friends and colleagues will have the deepest sympathy for his widow and daughter.—G. B. P

Surgeon Rear-Admiral ARTHUR RICHARD THOMAS, who served in the Royal Navy for 34 years, died at Southsea on October 30, aged 75. He was born at Portsmouth in 1876, the son of a Royal Naval captain, and educated at Portsmouth Grammar School. From there he went on to Guy's Hospital, qualifying in 1899. In 1913 he became a Fellow of the Royal College of Surgeons of Edinburgh. Entering the Royal Navy in 1901 as a surgeon, he reached the rank of surgeon captain in 1926. Five years later he was placed on the retired list, and was promoted to surgeon rear-admiral on the retired list in 1932. When H.M. Hospital Ship *Maine* was wrecked on the west coast of Scotland in June, 1914, Thomas played a conspicuous part in getting patients to safety and in the salvage of valuable stores. During the first world war he served in H.M.S. *Talbot* and was at the first landings at Gallipoli. Towards the end of 1915 he was stationed at the Royal Naval Hospital in Malta. For his valuable services, both in H.M.S. *Talbot* and at the R.N. Hospital, Malta, he was awarded the O.B.E. in 1919. After the war he served with the North Russia River Expeditionary Force, and in 1923 he was appointed medical officer-in-charge of R.N. Hospital, Portland. From 1926 to 1929 he was in charge of the surgical section of R.N. Hospital, Plymouth, and was appointed a year later professor of surgery at R.N. Hospital, Haslar, where he remained until he retired. During the last war he volunteered for re-employment in the rank of surgeon commander, and served as naval medical liaison officer at the E.M.S. Hospital, Park Prewett, Basingstoke, and later as the senior medical officer of a landing-craft base. His skill as a surgeon was of a very high order and he had considerable experience of orthopaedic surgery. He was a member of Council of the British Medical Association from 1932 to 1938, and he also served on a number of the Association's committees.

Dr. CHARLES HENRY COMERFORD, consultant physician in psychological medicine to Bexley, Greenwich, and Dartford group hospitals, and deputy physician-superintendent to Bexley Hospital, died suddenly at Bexley Hospital on November 4. He graduated in medicine at Trinity College, Dublin, in 1916, and proceeded M.D. in 1919. He took his D.P.H. in 1920 and his D.P.M. in 1924. In the war of 1914–18 he served with the R.A.M.C. in Salonika and France, and in 1922 joined the L.C.C. mental health service, serving at Cane Hill, Long Grove, Hanwell, and Bexley Hospitals. At the time of his death he had been at Bexley Hospital continuously for over 21 years. By his acquaintances he will be mainly remembered as a most amusing and charming companion—indeed, his wit and humour were remarkable, and always kindly—but his many friends will value most the memory of his innumerable acts of kindness and his genius for making friends and keeping up his friendships. He was a shrewd and conscientious physician and the most loyal and reliable of colleagues, being greatly beloved both in the hospital and among a widespread circle of friends and colleagues outside. In 1924 he married Charity Henderson, to whom our deepest sympathy is extended.

Medico-Legal

FORGED PRESCRIPTION FOR AMPHETAMINE

A woman pleaded guilty on October 4 at Rotherham Borough Court to a charge of attempting to obtain 100 amphetamine tablets by means of a forged instrument.[1] According to the prosecution, she visited her doctor and obtained a prescription for 50 amphetamine tablets. She took it to the chemist, who, finding it had been altered, made up the prescription for 50 tablets. On her asking him how many tablets he had given her, the chemist said 50. She pointed out that the prescription said 150. The chemist replied that he thought the doctor had prescribed only 50 tablets, and the woman said the doctor had altered the prescription because she was going on holiday.

The court discharged her absolutely.

1 *Yorkshire Evening Post*, October 4.

Medical Notes in Parliament

Pregnancy and Catholicism

Mr. R. W. SORENSEN asked the Minister of Health on November 15 to take steps to enable pregnant women to change their doctors for religious reasons. Mr. H. F. C. CROOKSHANK replied that there was nothing to prevent such changes being made. Pursuing the point, Mr. Sorensen requested that the Minister give some guidance to local authorities and mothers, both Catholic and Protestant. Mrs. JEAN MANN asked Mr. Crookshank to consider urging attendance at antenatal clinics, where, she said, the controversy would greatly resolve itself, and Colonel RALPH CLARK reminded the Minister that in such cases there might also be severe conflict of loyalties between duty to their religion and duty to their patients among doctors and nurses. Mr. SORENSEN gave notice that he would raise the matter again as soon as possible because he considered the replies given quite inadequate.

Housing Priority

Mr. H. MACMILLAN said in reply to a question on November 13 that local authorities had a statutory duty to give a reasonable preference to those living under unsatisfactory housing conditions. They had been requested to give due weight to claims made on the grounds of ill-health, including pulmonary tuberculosis.

D.D.T. Supplies

Mr. R. W. SORENSEN asked the Secretary of State for Foreign Affairs on November 14 what was being done by the United Nations Organization and W.H.O. to ensure a better supply and a more equitable distribution of D.D.T. In reply Mr. H. A. NUTTING told him that the Economic and Social Council of the United Nations was setting up a working party to examine the position and that the party was due to meet in February, 1952.

Alien in the Health Service

Mr. E. H. KEELING on November 15 asked the Minister of Health if he would make a statement about the employment as a clerk in the National Health Executive Council for Middlesex of a man who, having been a secret agent of the Czechoslovak Government, had been deprived of his British citizenship earlier in the year at the instance of the Attorney-General. Mr. H. F. C. CROOKSHANK replied that he was employed for a short time as a temporary clerk by the Middlesex Executive Council.

Cancer Cure Claim

Mr. PETER FREEMAN on November 15 asked the Minister of Health whether inquiries into the claims of Mr. Rees Evans for curing cancer had been concluded, and when a report could be expected. Mr. H. F. C. CROOKSHANK said in reply that the committee had not quite completed its investigations and was unable to say how soon it would be able to report.

Leeds Regional Hospital Board

On November 15 Colonel H. STODDART-SCOTT asked how many of the 191 rooms in the Queen's Hotel, Harrogate, were being used by the Leeds Regional Hospital Board on November 1, how many were occupied as a nurses' home, and how many were in use as a preliminary nurses' training school. Mr. H. F. C. CROOKSHANK replied that the board used 73 rooms. The principal sister tutor was using two rooms earmarked for the preliminary nurses' training school. No other rooms were at present used for the purposes of the school or the nurses' home, but 99 were earmarked for these purposes. The remainder were not considered suitable for use as living accommodation and would serve as stores.

Pneumoconiosis and Byssinosis

Mr. OSBERT PEAKE, on November 16, moving the second reading of the Pneumoconiosis and Byssinosis Bill, said the main object was to provide benefits out of the Industrial Injuries Insurance Fund for those totally disabled or for dependants of those dying from these diseases whose compensation claims had been barred by the time limits imposed in the past. The Bill would also improve the position of those who came within the two benefit schemes. Inclusion of partial disablement cases, most of which were at present in regular employment, would involve difficulty in ascertaining what loss of earning capacity had been suffered and the medical panels would have thrown on them a burden which they could not discharge. After the war, when these panels became overloaded with applications, they had to be diluted with doctors who were not fully expert in this subject.

Dr. EDITH SUMMERSKILL said the diagnosis of these diseases in the early stages had baffled the medical profession. Unfortunately *x*-ray examination did not reveal the condition in its early stages. If the partially disabled were included, provision would have to be made for examination of every miner and ex-miner, but the medical boards were very busy and the number of chest specialists available was limited.

Mr. EDWIN LEATHER welcomed the Bill, but told of a miner who went down with pneumonia, was radiographed, and was then told he must have had pneumoconiosis for at least 15 years. He could do only light work. He asked how much he would be allowed to earn and still come within the conditions of the Bill. Pneumonia was one of the most common causes of the discovery of the disease. He had been assured by the former Minister of Fuel and Power that a scheme for the compulsory *x*-ray examination of miners was in the pilot stage. It would take six months or a year to get it working. It might be practicable for an initial screening to be made by the doctors in each coalfield.

Dr. SUMMERSKILL intervened to say that the ordinary doctor could not interpret an *x*-ray plate. She added that a doctor employed by a Government department was a doctor first. He was not a dishonest man just because he was a Civil Servant.

Mr. LEATHER said that, if there were insufficient doctors to deal with the patients, an effort must be made to find more doctors. Had anyone suggested looking to Germany for medical men? The Pneumoconiosis Research Unit had as sound a medical knowledge of this subject as anyone in the world, but he was not satisfied that Britain had explored the methods of mass diagnosis and radiography used in the United States.

Mr. JAMES GRIFFITHS said that before 1948 men who claimed compensation and went to court were harried by doctors specially employed for the purpose. The whole thing was poisonous. He was glad that examination was revealing a case for the extension of the definition of pneumoconiosis to include emphysema. When he recently visited the silicosis clinic in the copper belt of Northern Rhodesia he felt ashamed when he saw the magnificent facilities for Africans and Europeans.

The Bill was read a second time without a division.

Switzerland.—Inquiries have been made of the Swiss Government, but so far without success, to secure reciprocal medical facilities for British subjects while in Switzerland.

Opticians.—The committee appointed to examine the need for the registration of opticians has finished taking evidence and hopes to present its report early next year.

The Services

The *London Gazette* has announced the award of the George Medal to Flight Lieutenant FRANCIS JOHN ENSELL, M.B., Ch.B., R.A.F., Royal Air Force Station, Biggin Hill. The citation reads as follows:

On August 23, 1951, a Harvard aircraft crashed into some dispersal pens on the edge of the aerodrome at Biggin Hill, and immediately burst into flames. The pilot, who was seriously injured, was trapped in the cockpit. Flight-Lieutenant ENSELL, Station Medical Officer, arrived with the ambulance and, despite the extreme danger to himself, went to the rescue of the trapped pilot. It was obvious that in his excited, half-conscious state the pilot would be difficult to extricate. Acting calmly and without hesitation, Flight-Lieutenant ENSELL administered morphine to the pilot and, as soon as this has quietened him, dragged him out of the cockpit, thereby saving his life. The whole of the interior of the aircraft was blazing furiously, the cockpit was full of smoke and flames, and there was an immediate danger of the petrol tank exploding. Flight-Lieutenant ENSELL stood beside the cockpit with the flames all round him and worked with completely calm efficiency at his rescue task. His shoes were badly scorched and his uniform ruined. Flight-Lieutenant ENSELL acted with great bravery and with no thought for his personal safety, and set an example of courage and devotion to duty of the highest order in risking his life to save that of a comrade.

Major-General Frederick Harris, C.B., C.B.E., *M.C.*, K.H.S., late R.A.M.C., has been appointed Director-General, Army Medical Services, with the rank of Lieutenant-General, and with effect from April 1, 1952, in succession to Lieutenant-General Sir Neil Cantlie, K.B.E., C.B., *M.C.*, K.H.S., late R.A.M.C.

CASUALTIES IN THE MEDICAL SERVICES

Previously reported missing, now known to be a prisoner of war.—Captain A. M. Ferrie, R.A.M.C.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending November 3 (No. 44).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending November 3					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	46	5	8	1	1	49	5	18	4	5	879	274	49
Deaths	—	—	—	—	—	—	—	—	—	—			
Dysentery	175	34	64	—	1	260	16	124	—	—	260	142	55
Deaths		—		—			—			—			
Encephalitis, acute	4	—	—	—		8	1	—	—		8	—	—
Deaths		—			—		—			—			
Erysipelas			17	3	2			29	4	4			
Food-poisoning	122	11		3		130	18		2				
Infective enteritis or diarrhoea under 2 years				24	35				18	25			
Deaths	11		2	1	—	6		3	—	1			
Measles*	1,993	65	85	169	172	7,815	512	131	71	119	7,815	3,374	496
Deaths		—	—	—	—		—	1	—	—			
Meningococcal infection	33	2	10	1	1	32	2	11	1	1	66	39	18
Deaths		—	—				2	1					
Ophthalmia neonatorum	57	1	9	—		35	2	10	1		85	61	35
Pneumonia, influenzal	510	49	6	2		433	30	6	7		678	496	419
Deaths (from influenza)†	17	3	3	—	1	19	4	—	—	1			
Pneumonia, primary			155					137					
Deaths	243	42		8	6	200	24		11	3			
Poliomyelitis, acute													
Paralytic	62	3	} 18	} —	} 7	} 204	} 12	} 18	} 9	} 2	} 330	} 27	} 10
Non-paralytic	20	2											
Deaths§	4	—			—	19	1			—			
Puerperal fever			7					5					
Puerperal pyrexia‖	242	30	4	1	1	59	5	5	3	1	155	117	59
Scarlet fever	1,067	117	296	30	44	1,108	82	193	63	70	3,385	1,819	1,108
Deaths		—	—	—	—		—	—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			139	31				153	42				
(2) Tuberculosis, non-respiratory			26	3				22	9				
(1) Deaths	} 155	{ 23	17	4	8	} 150	{ 25	26	4	6			
(2) Deaths		3	4	1	1		—	2	1	4			
Typhoid fever	2	—	—	—	1	—	—	2	2	6			
Deaths¶	—	—	—	—		—	—	—	—		62	15	5
Paratyphoid fever	26	—	—	—		5	—	—	—				
Whooping-cough	1,477	51	301	65	68	3,087	305	409	25	35	3,087	1,135	898
Deaths	1	—	1	—	—	4	—	—	—	—			
Deaths (0–1 year)	236	25	38	9	6	191	21	34	13	13	336	324	191
Deaths (excluding stillbirths)	5,180	850	549	99	131	5,025	767	602	110	134	5,308	4,373	4,171
Annual death rate (per 1,000 persons living)			11·3					12·1					
Live births	6,284	1,052	749	173	386	6,659	1,100	795	235	369	8,920	6,658	5,572
Annual rate per 1,000 persons living			15·4					16.0					
Stillbirths	168	24	29			163	17	22			273	193	163
Rate per 1,000 total births (including stillborn)			37					27					

* Measles not notifiable in Scotland and returns are approximate † Includes primary form for England and Wales, London, and N. Ireland § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Road Accidents in September

Road casualties in Great Britain during September totalled 19,810, including 438 killed and 4,753 seriously injured. There was the usual seasonal decrease compared with August, but the total was 450 more than that for the corresponding month last year. It was the highest figure for September since the war and only about 800 less than for September, 1938.

Infectious Diseases

Only small variations occurred in the incidence of infectious diseases in England and Wales during the week ending November 3. The largest was an increase of 91 in the notifications of acute pneumonia.

With the exception of Wales, a small rise in the number of notifications of acute pneumonia was recorded in every region of the country. The notifications of scarlet fever were 49 fewer than in the preceding week, but only very small changes occurred in the local returns; the largest was a decrease of 52 in Lancashire. The number of notifications of whooping-cough increased by 36, but no change of any size was reported in the local trends. The number of notifications of diphtheria was 11 more than in the previous week, and the total was the largest for 22 weeks. Four more cases of diphtheria were notified than in the preceding week in Lancashire and Durham. One-third of the total cases of diphtheria were notified in three areas; these were Liverpool C.B., Birmingham C.B., and Coseley U.D., each with 5 notifications. The notifications of measles were 31 in excess of the total of the preceding week; the largest of the local variations were an increase of 56 in Staffordshire and a decrease of 49 in Durham.

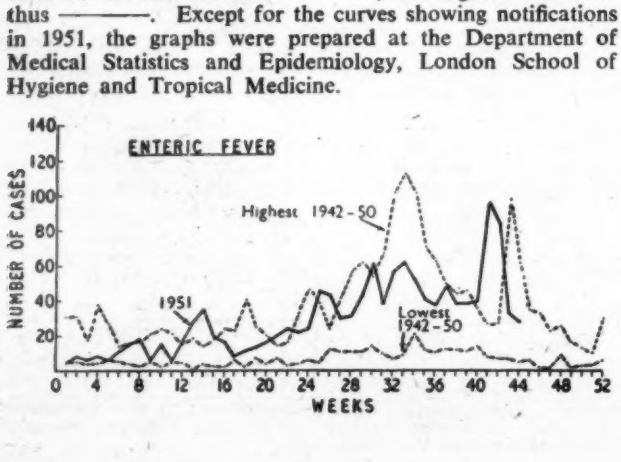
The number of notifications of paralytic acute poliomyelitis were the same as in the preceding week, while the number of non-paralytic cases declined by 14. The largest returns were Yorkshire West Riding 17 (Leeds C.B. 4), Lancashire 10, Warwickshire 6, London 5.

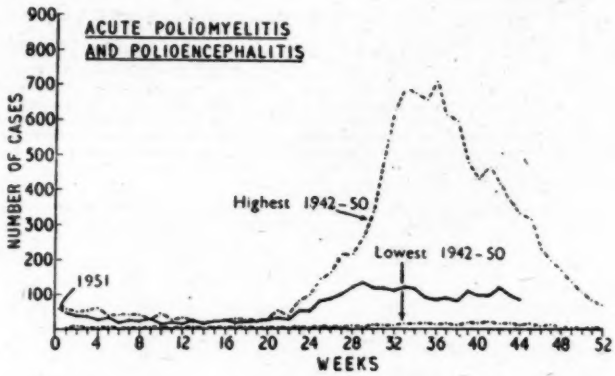
An increase of 24 was recorded in the number of notifications of dysentery. The largest rises during the week were Warwickshire, Birmingham C.B., from 1 to 14 and Lancashire from 17 to 32. Other large returns were London 34, Surrey 18, and Middlesex 14.

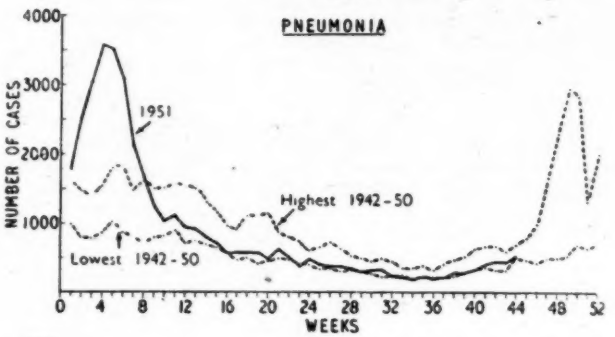
Of the 26 cases of paratyphoid fever 11 were notified in Lancashire (Liverpool C.B. 7). The largest outbreak of food-poisoning was 45 cases in Liverpool C.B.

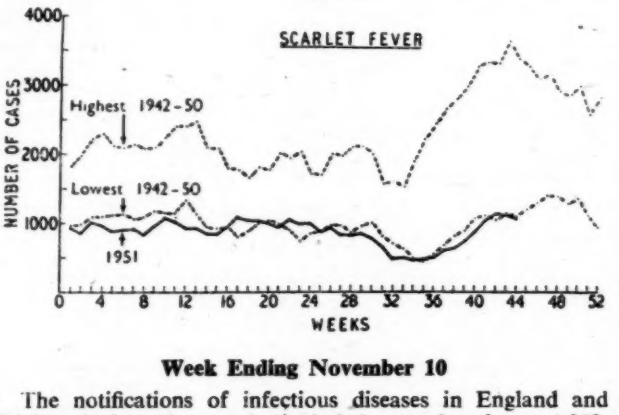
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending November 10

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,232, whooping-cough 1,625, diphtheria 42, measles, 1,935, acute pneumonia 479, acute poliomyelitis 78, dysentery 192, paratyphoid fever 10, and typhoid fever 4.

Medical News

"Any Questions?"

Early next month, in good time for Christmas, the first book of *"Any Questions?"* will be published. The book contains a selection of the best questions and answers which have appeared in the "Any Questions?" section of the *Journal* since the feature was started eight years ago. Many of these authoritative answers give practical information not yet in the textbooks. This book is confidently recommended to all practitioners. *"Any Questions?"* is strongly bound in cloth, small enough to fit the pocket, and costs 7s. 6d. (postage 6d.) Copies may be obtained on application to the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

"Clinical Journal" Ceases Publication

Owing to the increasing difficulties and expense of publication the *Clinical Journal* is suspending publication after the December issue until conditions improve.

George Medal for Medical Officer

On August 23 this year a Harvard training aircraft crashed at Biggin Hill R.A.F. station and burst into flames. The pilot was seriously injured and unable to get out of the cockpit, and the station medical officer, Flight Lieutenant F. J. Ensell, who was quickly on the scene in the ambulance, immediately gave him morphine and then extricated him from the wreck in spite of the flames and the risk that at any moment the petrol tank would explode. For this act he has now been awarded the George Medal (see the full citation on p. 1288). Flight Lieutenant Ensell is 25, and is a National Service medical officer who was called up in September, 1950. He was born in Birmingham and educated at the George Dixon Grammar School there from 1937 to 1943. He went on to the medical school of Birmingham University, where he qualified in 1949, and was called up after working for a year as house-surgeon at Birmingham General Hospital. Two airmen from the station fire brigade, who assisted in the rescue, received the King's Commendation for Brave Conduct.

Malaria in Korea and at Home

The prevailing form of malaria in Korea is benign tertian (*Plasmodium vivax*). British troops have been taking one tablet (100 mg.) paludrine daily during the malaria season and few cases of malaria have occurred. Paludrine is known to be a complete causal prophylactic for *Plasmodium falciparum*, but with *Plasmodium vivax* there is risk of malaria appearing after stopping paludrine. A number of reservists who have served in Korea throughout the malaria season are now returning to Britain and will shortly be back in civil life. It is not likely that many of these men will develop malaria, but the possibility should be borne in mind. (A full account of the recognition, treatment, and prevention of malaria will be found in the Refresher Course for General Practitioners published in this *Journal* on October 27, p. 1021.) The U.S. Army recently announced that as soon as supplies permit it is intended that all servicemen returning to America, whether malarial or not, will receive 1 g. chloroquine, followed by 14 daily doses of 15 mg. primaquine, the newly developed relative of mepacrine, which has proved curative in most Korean cases.

Annual Dinner of the Royal Free Hospital

The annual dinner of the Royal Free Hospital was held at the Savoy Hotel on November 7 under the chairmanship of Mr. J. Douglas McLaggan. The toast to the medical school and hospital was proposed by Sir William Gilliatt, who explained that when he was a student at the Middlesex he was attracted to the Royal Free by the outstanding reputation of the refreshments prepared by the women medical students on social occasions. As a result of his first visit to test the soundness of this reputation his connexion with the Royal Free was put on a permanent basis. Sir William surveyed the progress of the medical school from its early days—it was the first hospital to admit women medical students (in 1877) and the last hospital to admit men students (in 1947)—to the recent opening of new premises by the Queen, and he recalled some of the outstanding members of the staff. After Mr. D. F. Anderson, the hospital's treasurer, had replied, Dr. Doris Odlum, president of the Medical Women's Federation, proposed the health of the guests in an entertaining speech. Mr. James Stuart, Secretary of State for Scotland, said in reply that he was speaking not as a member of the Government but as an old friend of the hospital and medical school, of whose council he had recently been elected a member. His personal belief was that the medical profession should have as much freedom as possible from undue interference in the pursuit of their great work.

Presentation to Dr. J. B. Miller

On November 2 Dr. J. B. Miller, who was elected a Vice-President of the British Medical Association at the Annual Representative Meeting held at Southport last year and was Chairman of the Representative Body in 1946, 1947, and 1948, was presented with two easy chairs and a solid silver tea-service and salver by friends and patients in Bishopbriggs, Auchinairn, and Cadder, to celebrate his 50 years of practice in the Bishopbriggs district.

Greetings to Robert Doerr

Professor Robert Doerr celebrated his 80th birthday on November 1. He was born in Hungary in 1871, received his medical education in Vienna, and became professor of hygiene and bacteriology in the University of Basle in 1919. Professor Doerr is renowned as a bacteriologist and virologist, more especially for his investigations into sandfly fever and herpes encephalitis. He is the founder of *Archiv für die Gesamte Virusforschung*: he has edited the invaluable *Handbuch der Virusforschung*, and has now published seven monographs on immunity. At an age when most men have retired he is still intensely active. His many friends throughout the world have united to present to him, as a Festschrift, a special number of the *Archiv für Virusforschung*.

A Book for Christmas

50 Years of Medicine, containing in book form articles surveying the progress of medicine and surgery during the first half of this century which appeared in a special number of the *Journal* last year, is again available. Very pleasantly brought out, and handsomely bound, not only does it look impressive but the information it gathers together is useful and enlightening, and is of interest to both lay and medical readers. Over 300 pages of text, a complete index, and 32 illustrations make this a valuable book to have, and, incidentally, an excellent Christmas present. Costing 15s., *50 Years of Medicine* may be obtained through booksellers, or direct (post free) from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Bring Out Your Old Journals

The B.M.A. and the British Council recently helped to send Mr. C. Price Thomas, the chest surgeon, on an operating tour in Yugoslavia. One result of this visit was the realization that Yugoslavia is very short of up-to-date medical literature, and, although a number of free copies of various journals are being sent to libraries in Belgrade, Zagreb, and elsewhere, many more are needed. Readers who feel they would like to assist their Yugoslav colleagues, and incidentally increase British prestige, are invited to send used copies of British medical periodicals (e.g., *Thorax*, *British Heart Journal*, *British Medical Journal*, *Lancet*, etc.) to the Mailing Department, the British Council, 65, Davies Street, London, W.1, marked "For Overseas Distribution."

Emergency Bed Service: Applications and Admissions

During the seven days ending November 19 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 834, of whom 91% were admitted.

Wills

Surgeon Vice-Admiral Sir Robert William Basil Hall, of Haslemere, Surrey, left £16,908, including a number of legacies and the residue upon trust for his wife for life and then to the Royal Medical Benevolent Fund, apart from £2,500 of further legacies.

COMING EVENTS

Institute of Psychiatry

Details of the syllabus for the second term (beginning January 7) of the 1951–2 session lecture and demonstration courses for postgraduate students in psychiatry are now available. Mental testing, personality, genetics of mental disorder, psychopathology, and psychotherapy are among the subjects to be dealt with. All information from the secretary, Institute of Psychiatry, Maudsley Hospital, S.E.5.

Irish Medical Schools and Graduates' Association

The association dinner will be held at Rembrandt Hotel, S.W.7, on December 13 at 7.15 p.m., when the president, Sir William P. MacArthur, will be in the chair.

Leeuwenhoek Lecture

Dr. C. H. Andrewes, F.R.S., will deliver the Leeuwenhoek Lecture before the Royal Society (Burlington House, Piccadilly, London, W.) on Thursday, December 13, at 4.30 p.m. His subject is "The Place of Viruses in Nature."

Scientific Films

The medical committee of the Scientific Film Association has organized a showing of films of interest to physicians at the Wright–Fleming Institute of Microbiology, St. Mary's Hospital, W.2, on Wednesday, December 12, at 5 p.m., when it is hoped to show the following films: "Phagocytosis of Cocci by Polymorphs"; "Segmental Resection of the Lung in Bronchiectasis"; and "Thrombosis and Embolism."

Unestablished Practitioners Group

The annual general meeting will be held on November 29 at the Bonnington Hotel, Southampton Row, W.C.1, at 8.30 p.m. All practitioners with inadequate lists, and assistants in the general medical services, are invited to attend.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Rose Hertz Hall, Woburn House, Upper Woburn Place, W.C., November 25, 3 p.m., "*Human Genetics—Biochemical Abnormalities*" (illustrated by lantern slides), by Professor L. S. Penrose.

Monday

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—November 26, 8.30 p.m., "*The Place of Clinical Pathology in Changing Medicine*," discussion to be introduced by Dr. Cuthbert Dukes and Professor R. J. V. Pulvertaft.

OXFORD UNIVERSITY.—At Physiology and Biochemistry Lecture Room, Oxford, November 26, 12 noon, "*Experimental Human Starvation*," by Professor Ancel Keys (University of Minnesota).

●POSTGRADUATE MEDICAL SCHOOL OF LONDON, Hammersmith Hospital, Ducane Road, W.—November 26, 4 p.m., "*Methods of Assessing Cardiac Failure*," by Professor E. P. Sharpey-Schafer.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 26, 5.30 p.m., "*Selected Features of Applied Anatomy of the Orbit*," by Professor T. Nicol.

UNIVERSITY COLLEGE: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, London, W.C., November 26, 5.15 p.m., "*Anticholinesterases*" public lecture by Dr. W. S. Feldberg. (See also December 3.)

Tuesday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., November 27, 5.30 p.m., "*Viruses as Causes of Diseases*," by Professor S. P. Bedson.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 27, 5.30 p.m., "*Virus Infections*," by Dr. J. A. Dudgeon.

●ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—November 27, 5 p.m., "*Renal Failure*," by Dr. M. L. Rosenheim.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—November 27, 3.45 p.m., "*Sarcoma 37, Ascites Tumours and Some Aspects of Cancer Research*," Imperial Cancer Research Fund Lecture by Dr. James Craigie.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, November 27, 5 p.m., "*Medical Evidence*," by Mr. John Cameron.

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, London, W.—November 27, 5.30 p.m., neurological demonstration by Dr. Gerald Parsons-Smith.

Wednesday

●DAVIDSON CLINIC, 58, Dalkeith Road, Edinburgh.—November 28, 8 p.m., "*Psychology and War*," by Miss Jane Darroch, Ph.D.

EDINBURGH CLINICAL CLUB.—November 28, 4.30 p.m., clinical meeting by Dr. J Halliday Croom. Visit to the Dietetic Department, Edinburgh Royal Infirmary.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 28, 5.30 p.m., "*Mycology—Laboratory Diagnosis of Superficial Fungus Infections*," by Dr. R. W. Riddell.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., November 28, 4.30 p.m., "*Acute Retention of Urine*," by Mr. H. K. Vernon.

●LONDON MARRIAGE GUIDANCE COUNCIL, 78, Duke Street, Grosvenor Square, W.—November 28, 6 p.m., "*The Parenthood Relationship*," by Dr. Ethel Dukes.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON, Hammersmith Hospital, Ducane Road, W.—November 28, 11.45 a.m., Medical Clinical-pathological Conference.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 28, 5.30 p.m., "*Fundus Appearances in Vascular Disease*," by Mr. R. P. Crick.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—November 28, 5 p.m., "*Intracardiac Surgery*," Dr. John Burns Lecture by Mr. R. C. Brock. Medical practitioners are invited.

Thursday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., November 29, 5.30 p.m., "*Current Knowledge on Nature of Viruses*," by Mr F. C. Bawden.

CHRISTIAN MEDICAL FELLOWSHIP.—At Royal Empire Society, Northumberland Avenue, London, W.C., November 29, 7.45 for 8.15 p.m., "*The Christian Faith in Medical Practice*," by Professor John Kirk.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY, The Union, University Avenue, Glasgow.—November 29, 7.30 p.m., "*Arteriovenous Communications*," by Sir James Learmonth.

HONYMAN GILLESPIE LECTURE.—At University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh, November 29, 5 p.m., "*Clearance Tests of Renal Function*," by Mr. C. P. Stewart, M.Sc., Ph.D.

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—November 29, 5 p.m., "*Minor Medical Problems*," by Dr. J. H. Gibbens.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 29, 5.30 p.m., "*Histopathology—Cellular Naevi and Melanomas*," by Dr. H. Haber.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—November 29, 3 p.m., "*Metabolism and Cerebral Function*," by Dr. Derek Richter.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool.—November 29, 8 p.m., ordinary meeting. "*Phaeochromocytoma of the Adrenal Medulla*," by Mr. L. R. Broster.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8, Hunter Street, Brunswick Square, W.C., November 29, 8.30 p.m., "*Cancer and the Public—The Need for Education*," discussion to be opened by Mr. Malcolm Donaldson, Professor Sidney Russ, and Dr. John Walter. All visitors welcome.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 29, 5 p.m., "*Demyelinating Diseases in Ocular Practice*," by Dr. S. Nevin.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, November 29, 5 p.m., '*Observations on the Local Effects of Cold on the Circulation*," by Professor A. D. M. Greenfield.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—November 29, 4.30 p.m., lecture-demonstration in neurology by Dr. D. Williams.

WELSH NATIONAL SCHOOL OF MEDICINE.—At Reardon Smith Lecture Theatre, Park Place, Cardiff, November 29, 8 p.m., "*University Education and Medicine*," inaugural address by Professor H. Scarborough.

Friday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 30, 5.30 p.m., "*Lichen Planus and Lichenoid Eruptions*," clinical demonstration by Dr. S. Thomson.

●MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—November 30, 6.45 p.m., cocktail party.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON, Hammersmith Hospital, Ducane Road, W.—November 30, 11.15 a.m., Surgical Clinical-pathological Conference; 2 p.m., *"The Evaluation of Modern Methods in the Treatment of Prostatic Obstruction,"* by Mr. A. Clifford Morson; 4 p.m., *"Iron and Anaemia,"* by Dr. Sheila Callender.

●ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—November 30, 5 p.m., *"Advances in the Treatment of Tuberculosis,"* Dr. F. P. Lee Lander.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 30, 5.30 p.m., *"The Endocrines and the Eye,"* by Dr. C. A. Keele.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—November 30, 8 p.m., *"Old Age: A Medical Problem,"* by Mr. G. A. G. Crease.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Consultant Psychiatrist St. Andrew's Mental Hospital, Norwich*, J. M. Rosie, M.D., D.P.M. *Registrar in Psychiatry, Little Plumstead Mental Deficiency Colony*, J. Mukerjee, M.B, *Medical Officer, Regional Blood Transfusion Unit*, E. M. Sewell, M.B., Ch.B., D.P.H. *Senior Registrar in Psychiatry, Little Plumstead Mental Deficiency Colony*, R. C. MacGillivray, M.B., Ch.B., F.R.F.P.S. *Anaesthetic Registrar, United Norwich Hospitals*, C. J. Coghlan, M.B., B.Ch. *Ear, Nose and Throat Registrar, Norfolk and Norwich Hospital*, D. G. Jones, M.R.C.S., L.R.C.P.

HAGEDORN, E. O., L.R.C.P.&S.Ed., Deputy Medical Superintendent, Littlemore Hospital, Oxford.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Part-time Consultant Paediatric Surgeon, with a special interest in Thoracic Surgery*, D. J. Waterston, M.B., Ch.B., F.R.C.S. *Assistant Radiologist*, G. N. Weber, M.R.C.S., L.R.C.P., D.M.R.D. *House-surgeon to Orthopaedic, and Plastic Departments (Senior House Officer Grade)*, F. E. Weale, M.B., B.S. *Junior Resident Anaesthetist (Senior House Officer Grade)*, Colette L. Raulin, M.B., B.S.

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Consultant Pathologist, Newsham General and Mill Road Maternity Hospitals*, R. Y. Dawbarn, M.D. *Consultant Paediatrician to Hospitals in Central Wirral Area*, K. R. Llewellin, M.R.C.P., D.C.H. *Whole-time Assistant Psychiatrist, Upton Mental Hospital*, L. Couper, M.B., Ch.B., D.P.M. *Whole-time Assistant Radiologist, East Liverpool Area*, E. G. Donovan, M.B., Ch.B., M.R.C.P., D.M.R.D., D.C.H., C.P.H. *Whole-time Assistant Anaesthetist for duties at Hospitals mainly in South Liverpool and St. Helens Area*, H. J. Weldon, M.B., B.Ch., D.A.

MONRO, ALAN BENTLEY, M.D., D.P.M., Physician-superintendent and Consultant Psychiatrist, Long Grove Hospital, Epsom, Surrey.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Part-time, Anaesthetist, St. Mary's Hospital, Plaistow*, G. Herington, M.B., B.S., D.A. *Full-time Psychiatrist, Runwell Mental Hospital*, D. W. Liddell, M.B., B.S., M.R.C.P., D.P.M. *Part-time Physician in Physical Medicine, Enfield Group of Hospitals*, R. M. Mason, B.M., B.Ch., M.R.C.P. *Part-time Anaesthetist, Invalid and Crippled Children's Hospital*, J. W. Monro, M.B., B.Chir., D.A. *Part-time Anaesthetist, Prince of Wales's Hospital*, P. H. Moore, M.R.C.S., L.R.C.P., D.A. *Part-time Paediatrician, Poplar Hospital*, D. Morris, M.R.C.S., M.R.C.P., D.C.H. *Part-time Obstetrician and Gynaecologist, Wanstead Hospital*, F. L. E. H. Musgrove, M.D., D.A., M.R.C.O.G. *Part-time Gynaecologist, Forest Hospital*, R. C. Percival, F.R.C.S., M.R.C.O.G. *Part-time Physician in Physical Medicine, Hertford County, Haymeads, and Bishop's Stortford Hospitals*, M. E. Wigfield, M.B., B.S., D.Phys.Med. *Part-time Anaesthetist, Queen Elizabeth Hospital for Children*, Gertrude A. Willis, M.B., Ch.B., D.A.

NORTHERN IRELAND HOSPITALS AUTHORITY.—*Assistant Administrative Medical Officer*, C. W. Kidd, M.D. *Physician, Armagh and Banbridge Area*, T. T. Fulton, M.D., M.R.C.P. *Second Surgeon, Tyrone and Fermanagh Areas*, W. F. Smyth, M.B., B.Ch., F.R.C.S.Ed. *Relief Surgeon, based on Belfast City Hospital*, W. H. Ekin, M.B., B.Chir., F.R.C.S.Ed., D.P.H.

RUSSELL, A. WILSON, M.D., D.P.H., Consultant Chest Physician, Walsall Group of Hospitals and Walsall County Borough.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brockis.—On November 11, 1951, to Muriel (formerly Maney), wife of J. Gwynne Brockis, F.R.C.S., 14, Rokeby Drive, Newcastle-upon-Tyne, a son—Andrew John.

Oldham.—On October 31, 1951, at the Carmarthen Maternity Unit, to Valerie (formerly Williams), wife of Dr. William Oldham, a son.

MARRIAGES

Armstrong—Poutiainen.—On November 17, 1951, at Helsinki, Finland, Dr. James Grant Armstrong, of Basingstoke, Hants, to Leena-Maija Poutiainen, of Helsinki.

DEATHS

Allen.—On November 11, 1951, at "Riversdale," Bridge Street, Belper, Derbyshire, Richard Clayton Allen, M.R.C.S., L.R.C.P., D.P.H., J.P., aged 69.

Carmichael.—On November 16, 1951, Norman Scott Carmichael, M.B., F.R.C.P.Ed., of 43, Moray Place, Edinburgh.

Dixon.—On November 13, 1951, at 20, Queens Gardens, Herne Bay, Kent, William John Dixon, M.B., C.M., late of Malaya.

Fulham-Turner.—On November 16, 1951, at Hastings, Sussex, Harry Fulham-Turner, M.R.C.S., L.R.C.P., late of Muswell Hill, London, N.

Gardner.—On November 14, 1951, Eric Gardner, M.B., B.Ch., of Portmore House, Weybridge, Surrey.

Gordon.—On November 11, 1951, at his home, Beau Désert, St. Saviour's, Jersey, Colin Gordon, M.B., C.M.

McCall.—On November 10, 1951, at Donnington House Nursing Home, Camberley, Surrey, Eva McCall, M.D., D.P.H.

Risdon.—On November 18, 1951, at "Merivale," St. Alban's Avenue, Bournemouth, William Elliot Risdon, M.D., aged 87.

Smallwood.—On November 13, 1951, at Wheathampstead, Herts, Matthew Edmund Smallwood, M.R.C.S., L.R.C.P.

Walmsley.—On November 12, 1951, at his home, Ardmore, Armagh, Northern Ireland, Thomas Walmsley, M.D., aged 62.

Any Questions?

Book of "Any Questions?"

Q.—*When will the book "Any Questions?" be ready, and how can I get a copy?*

A.—The first collection of *Any Questions?* will be published in book form early in December. The book consists of a selection of the best questions and answers which have appeared in this section of the *Journal* since the feature was started in February, 1943. The book costs 7s. 6d. (postage 6d.), it is fully indexed, and contains 268 pages. Orders may be placed now with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

Dysmenorrhoea at the Wedding

Q.—*A girl who suffers from severe dysmenorrhoea (to the extent of occasionally fainting) finds that her wedding day is going to clash with the expected date of her period. For social reasons she cannot defer the wedding. (1) Can her period be delayed or accelerated, and is this advisable? (2) If not, what drug treatment is advised to tide her over the wedding?*

A.—The difficulty with this sort of problem is that no woman has a cycle which is so regular that the onset of the next period can be accurately predicted to a day. Moreover, the various emotional changes associated with marriage and the preparations for it not infrequently disturb menstruation, making it late or early. The chance that the dates will not clash is so high that it is doubtful whether it is worth while attempting to postpone the expected period, but rather one should hope they will not and be prepared to treat the dysmenorrhoea if they do. In this case amphetamine sulphate might be effective. A suitable dose is 10 mg. given orally at the onset of the period, and repeated in four hours if necessary. It would be wise, however, to give a test dose of 2.5 mg. at any earlier date to exclude any idiosyncrasy to the drug.

If it is decided to try to postpone the period, then an oestrogen such as ethyl oestradiol 0.05 mg. t.d.s. could be given every day for the month preceding marriage—i.e., starting at the conclusion of the previous period. Once the marriage is over, treatment should be stopped, and menstruation is then likely to begin 2 to 10 days later. The disadvantage of this is that the postponed period may be unduly prolonged and heavy, but on the other hand it will almost certainly be painless, because the oestrogen is likely to have suppressed ovulation during the cycle of its administration. If it is already too near the wedding day to give this full course of treatment, then progesterone 20 mg. intramuscularly daily could be given, starting seven days before the expected period and continuing up to and including the day of the wedding. Menstruation is likely to begin two to four days after stopping this treatment and will probably be as painful as usual.

Citrated Blood

Q.—*(a) What is known of the metabolism of exogenous sodium citrate? (b) Have toxic symptoms ever resulted from its use as an anticoagulant in intravenous therapy?*

A.—*(a)* It is probable that sodium citrate can enter the cells and undergo breakdown to pyruvate, hence to "active acetate," which could then be oxidized by way of the citric cycle mechanism. Intravenous injection of citrate leads to the formation of calcium citrate, which, since it does not ionize, would cause a fall in ionic calcium in the blood. This is normally countered by withdrawal of calcium from bones and teeth, but, if large doses of citrate are administered, might lead temporarily to tetany.

(b) The administration of large amounts of citrate to human beings very seldom produces toxic effects. It has

been shown that during citrate infusions the plasma calcium concentration does in fact increase, and this doubtless tends to maintain the concentration of ionized calcium. The fastest rates of citrate administration are reached in exchange transfusion of newborn infants. Yet even under these conditions, provided the dosage does not exceed about 200 mg. of citrate per kg. per hour, toxic signs are not seen. This is equivalent to about 200 mg. of disodium citrate, or 75 ml. of citrated blood, per kg. per hour. If the dosage reaches about 400 mg. of citrate per kg. per hour, tetany is sometimes observed unless calcium gluconate is given prophylactically. In adults it is probably safe to ignore the possibility of citrate toxicity until a dose of 5 litres of citrated blood per hour is exceeded. It should be added that it is possible to kill animals by injecting citrate into them at rates in excess of those quoted.

Encephalitis Lethargica

Q.—*How may encephalitis lethargica be diagnosed in the acute stage? Is there any evidence that treatment with antibiotics is likely to be of value either then or to lessen the risk of late sequelae? If so, which antibiotics are recommended, and in what dosage?*

A.—The diagnosis of acute encephalitis lethargica is essentially a clinical one, and there is no confirmatory pathological test at present available. The disease in an acute form has been uncommon in the United Kingdom during the past 20 years, the diagnosis is difficult, and some cases are recognized only when post-encephalitic parkinsonism develops at a later date. Even during the epidemics of the disease the clinical picture varied a good deal in different years. Points suggestive of acute encephalitis lethargica are reversal of the normal sleep rhythm, ocular palsies, myoclonic movements, persistent hiccups, and extrapyramidal rigidity occurring in the setting of an acute illness. The cerebrospinal fluid may be normal or may contain an excess of lymphocytes. No antibiotic has as yet been shown to be of value in the acute stages of the disease or to lessen the risk of sequelae.

Green Potatoes

Q.—*I have been told that I ought not to eat potatoes which show any green on the skin. Is this true, and, if so, why?*

A.—When potatoes sprout, a poison known as solanin is produced. The development of a green colour on the skin often indicates a tendency to sprout. It is most unlikely that serious poisoning would be caused by a small portion of cooked green potato, but it would be unwise to eat substantial amounts.

Food Value of Breakfast Cereals

Q.—*What are the food value and vitamin content of breakfast cereals? How are they prepared?*

A.—Breakfast cereals consist mainly of carbohydrate, and as such form a useful supplementary source of calories, providing between 90 and 110 calories per ounce (30 g.). They also contain some protein and small amounts of fatty and mineral matter. The content of B vitamins depends upon the proportion of the germ employed, larger proportions resulting in a higher content of these vitamins. When bran is incorporated the nicotinic acid content is considerably increased, though it has to be remembered that the former is not easily digested and functions mainly as a laxative. Riboflavin is low in all the cereal products, and the vitamin B_1 content will depend on the mode of preparation of the cereal. Vitamins A and D are not present in cereals to any appreciable extent.

Breakfast cereals are prepared by various drying, grinding, rolling, and baking processes. Cornflakes, for example, consist of cooked maize treated with malt-honey and subsequently dried, rolled, and baked. Other breakfast cereals are made from wheat and usually include the whole grain. Oatmeal is made by simply cleaning and grinding oats, and "groats" consist of oats from which the husks have been completely removed. Oats are also prepared by rolling processes.

Aetiology of Facial Hirsutism in Women

Q.—*During the last few months a woman of 30 has developed a considerable growth of hair on her upper lip and chin. There are no other obvious signs of endocrine disorder. What are the likely causes of this, and how should the case be investigated?*

A.—The problem of hair on the lip and chin in women is one of considerable difficulty, particularly from the therapeutic angle. Most women face this problem in some degree, since, as with many other features, there is a representation of male characteristics in the female in a minor or vestigial degree. Our attitude to-day requires reorientation. Some races—e.g., Celts—are more prone to it than others, and the tendency runs in some families as an inherited or innate characteristic. It may manifest itself at puberty, during pregnancy, in the climacteric, or in senility; or it may gradually grow in extent and degree throughout life. Where it is unassociated with adiposity, amenorrhoea, or oligomenorrhoea, it must be labelled as idiopathic or constitutional, although in actual fact there may be an adrenal androgenic element here too. Where amenorrhoea and adiposity are present, it becomes part of an adrenogenital syndrome or occasionally of a Cushing's syndrome. The investigations would include estimation of the urinary 17-ketosteroids, although normal values do not rule out adrenal hyperactivity. An intravenous pyelogram might indicate an adrenal tumour. In most cases of uncomplicated hirsutism in women, however, all investigations will prove to be negative or lacking any positive indications.

Dysphagia and Cancerophobia

Q.—*Dysphagia is frequently associated with a fear of cancer in my experience. What is the explanation of this—does dysphagia, from whatever cause, arouse a fear of cancer, or does the patient who fears cancer tend to localize his phobia to the throat?*

A.—Dysphagia comes first and the fear of cancer follows. The former is often induced by some trivial event such as oesophagitis following influenza or arising from reflux of acid into the gullet. Naturally there are exceptions to this rule, especially where a nervous patient has heard of someone suffering from carcinoma of the gullet.

NOTES AND COMMENTS

Conception Without Penetration.—Dr. J. L. KEARNS (London) writes: I disagree with the answer to this question ("Any Questions?" November 10, p. 1166). In a small general practice with few maternity and gynaecological cases to deal with in the year 1929, I remember two cases in young women: one was made pregnant through artificial silk knickers, having an introitus not larger than ¼ in. in diameter, after one attempt only at intercourse. Another without knickers, introitus about the same size, became pregnant after more than one intercourse without rupture of the hymen. Surely a lot depends on the youth of the pair, strength of ejaculation, and permeability of clothing, irrespective of depth of penetration.

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